



(22) Date de dépôt/Filing Date: 2011/04/21

(41) Mise à la disp. pub./Open to Public Insp.: 2011/10/27

(45) Date de délivrance/Issue Date: 2023/01/24

(62) Demande originale/Original Application: 2 796 561

(30) Priorité/Priority: 2010/04/21 (US61/326602)

(51) Cl.Int./Int.Cl. *C12Q 1/68* (2018.01),
A61K 38/37 (2006.01), *C12Q 1/6827* (2018.01),
C12Q 1/6858 (2018.01), *C12Q 1/6876* (2018.01),
G01N 33/483 (2006.01), *C07K 14/755* (2006.01)

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(54) Titre : FACTEURS GENETIQUES ASSOCIES A UN DEVELOPPEMENT D'INHIBITEURS DANS L'HEMOPHILIE A

(54) Title: GENETIC FACTORS ASSOCIATED WITH INHIBITOR DEVELOPMENT IN HEMOPHILIA A

(57) Abrégé/Abstract:

The present invention provides methods for predicting the risk of an individual developing antibodies to factor VIII by identifying a single nucleotide polymorphism of an immune response or immune modifier gene. The invention further provides oligonucleotides, diagnostic kits, microarrays, and isolated nucleic acids comprising single nucleotide polymorphisms of immune response or immune modifier genes.

ABSTRACT

The present invention provides methods for predicting the risk of an individual developing antibodies to factor VIII by identifying a single nucleotide polymorphism of an immune response or immune modifier gene. The invention further provides oligonucleotides, 5 diagnostic kits, microarrays, and isolated nucleic acids comprising single nucleotide polymorphisms of immune response or immune modifier genes.

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 191

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JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 191

NOTE: For additional volumes, please contact the Canadian Patent Office

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GENETIC FACTORS ASSOCIATED WITH INHIBITOR DEVELOPMENT IN HEMOPHILIA A

[0001] This is a divisional application of Canadian patent application Serial No. 2796561, filed on
5 April 21, 2011.

BACKGROUND OF THE INVENTION

[0002] Blood coagulation is a complex and dynamic biological process that depends on a
series of interdependent biochemical reactions. Coagulation factor VIII (FVIII) is a key
10 component of the blood coagulation cascade.

[0003] When a bleed occurs, FVIII is directed to the bleeding site and forms a Xase complex
with activated factor IX (FIXa) and factor X (FX). The Xase complex activates FX, which in
turn activates prothrombin to thrombin, which activates other components in the coagulation
cascade to generate a stable clot (reviewed in Saenko *et al.*, *Trends Cardiovasc. Med.*, 9:185-192
15 (1999); Lenting *et al.*, *Blood*, 92:3983-3996 (1998)).

[0004] In hemophilia A, a congenital X-linked bleeding disorder characterized by a deficiency
in FVIII, the lack of functional FVIII hampers this positive feedback loop, resulting in
incomplete coagulation, which manifests as bleeding episodes of increased duration rather than
increased intensity (Zhang *et al.*, *Clinic. Rev. Allerg. Immunol.*, 37:114-124 (2009)).

20 [0005] The severity of hemophilia A varies based on the nature of any mutation to FVIII and
the extent of function of any endogenous FVIII that is formed. About two thirds of patients have
"severe" hemophilia, characterized as less than 1% functional FVIII. Patients with "moderate"
hemophilia have about 1-5% functional FVIII, and patients with "mild" hemophilia have about
5-50% of normal FVIII function (Zhang *et al.*, *Clinic. Rev. Allerg. Immunol.*, 37:114-124
25 (2009)). Current treatment for hemophilia typically consists of factor VIII replacement therapy,
in which the patient receives recombinant or plasma-derived factor VIII to prevent or treat
bleeding episodes. However, in approximately 25-30% of patients with severe hemophilia A and
in approximately 5% of patients with mild to moderate hemophilia A, inhibitory alloantibodies
are produced against FVIII, abrogating the effectiveness of this treatment (Oldenburg and
30 Pavlova, *Haemophilia*, 12 (suppl. 6):15-22 (2006)).

[0006] Inhibitor development is considered to be the most significant complication in the treatment of hemophilia. Patients with inhibitors have a higher mortality rate because their bleeding episodes become more difficult and costly to treat, and preventative treatment is generally not possible in these patients. In patients with high-titer inhibitors, there is an increased risk of developing recurrent bleeding in particular joints, which may ultimately result in decreased quality of life, disability, or death from excessive blood loss (Zhang et al., *Clinic. Rev. Allerg. Immunol.*, 37:114-124 (2009); Gouw and van den Berg, *Semin. Thromb. Hemost.*, 35:723-734 (2009)). Although in some cases immune tolerance induction can eradicate FVIII inhibitors in patients with hemophilia A, relapse is possible and not all patients reach immune tolerance (Wight et al., *Haemophilia*, 9:436-463 (2003)).

[0007] Accordingly, there is a need in the art for the identification of genetic markers that are associated with increased likelihood of developing inhibitory antibodies to FVIII and for corresponding methods of identifying the presence of these genetic markers in hemophiliac patients. Prior or early identification of such genetic markers could lead to dose and/or timing adjustments and to the use of alternative therapies to avoid the development of antibodies to FVIII.

BRIEF SUMMARY OF THE INVENTION

[0008] In one aspect, the present invention provides a method for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, the method comprising the steps of: (a) detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4, in a biological sample from the individual; and (b) predicting the risk of the individual of developing antibodies to FVIII. In a preferred embodiment, the at least one SNP is selected from those listed in Table 3. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712.

[0009] In a second aspect, the present invention provides a method for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with severe Hemophilia, the method comprising the steps of: (a) detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2

and a SNP listed in Table 4, in a biological sample from the individual; and (b) predicting the risk of the individual of developing antibodies to FVIII. In a preferred embodiment, the at least one SNP is selected from those listed in Table 4. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888.

[0010] In a third aspect, the present invention provides a method for assigning treatment comprising administration of Factor VIII (FVIII) to an individual diagnosed with Hemophilia, the method comprising the steps of: (a) detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4, in a biological sample from the individual; and (b) predicting the risk of the individual of developing antibodies to FVIII, and (c) assigning therapy comprising administration of Factor VIII to the individual. In a preferred embodiment, the at least one SNP is selected from those listed in Table 3. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712.

[0011] In a fourth aspect, the present invention provides a method for assigning treatment comprising administration of Factor VIII (FVIII) to an individual diagnosed with severe Hemophilia, the method comprising the steps of: (a) detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4, in a biological sample from the individual; and (b) predicting the risk of the individual of developing antibodies to FVIII, and (c) assigning therapy comprising administration of Factor VIII to the individual. In a preferred embodiment, the at least one SNP is selected from those listed in Table 4. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888.

[0012] In a fifth aspect, the present invention provides a method for assigning treatment comprising administration of Factor VIII bypass therapy to an individual diagnosed with Hemophilia, the method comprising the steps of: (a) detecting the presence of at least one single

nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4, in a biological sample from the individual; and (b) predicting the risk of the individual of developing antibodies to FVIII, and (c) assigning therapy comprising administration of Factor VIII bypass therapy to the individual. In a preferred embodiment, the at least one SNP is selected from those listed in Table 3. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712.

[0013] In a sixth aspect, the present invention provides a method for assigning treatment comprising administration of Factor VIII bypass therapy to an individual diagnosed with severe Hemophilia, the method comprising the steps of: (a) detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4, in a biological sample from the individual; and (b) predicting the risk of the individual of developing antibodies to FVIII, and (c) assigning therapy comprising administration of Factor VIII bypass therapy to the individual. In a preferred embodiment, the at least one SNP is selected from those listed in Table 4. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888.

[0014] In a seventh aspect, the present invention provides a diagnostic kit for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, the kit comprising at least one oligonucleotide capable of being used to detect at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4. In a preferred embodiment, the at least one SNP is selected from those listed in Table 3. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712.

[0015] In an eighth aspect, the present invention provides a diagnostic kit for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with severe Hemophilia, the kit comprising at least one oligonucleotide capable of being used to detect at

least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4. In a preferred embodiment, the at least one SNP is selected from those listed in Table 4. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888.

[0016] In a ninth aspect, the present invention provides a microarray for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, the microarray comprising a support having a plurality of discrete regions, each discrete region having a nucleic acid fragment spotted thereon, wherein at least one nucleic acid fragment spotted on the support comprises a sequence that is complementary to a genomic sequence that flanks a single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4. In a preferred embodiment, the at least one SNP is selected from those listed in Table 3. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712.

[0017] In a tenth aspect, the present invention provides a microarray for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with severe Hemophilia, the microarray comprising a support having a plurality of discrete regions, each discrete region having a nucleic acid fragment spotted thereon, wherein at least one nucleic acid fragment spotted on the support comprises a sequence that is complementary to a genomic sequence that flanks a single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4. In a preferred embodiment, the at least one SNP is selected from those listed in Table 4. In another preferred embodiment, the at least one SNP is selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888.

[0017A] The present invention as claimed relates to:

- (1) A method for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, the method comprising the steps of (a) detecting the presence of one or more single nucleotide polymorphisms (SNPs) in a biological sample from the individual, wherein the one or more SNPs comprises T>C variant at SNP rs13206518, wherein presence of the T>C variant at SNP rs13206518 indicates an decreased risk of the individual developing antibodies to FVIII; and (b) predicting the risk of the individual of developing antibodies to FVIII based on the one or more SNPs;
- (2) The method of (1) above, wherein an odds ratio of less than 1 from the one or more SNPs collectively is predictive of a decreased risk of developing antibodies against FVIII and an odds ratio of more than 1.0 from the one or more SNPs collectively is predictive of an increased risk of developing antibodies against FVIII;
- (3) The method of (1) or (2) above, wherein the individual either (i) has not received therapy comprising administration of FVIII, or (ii) has received therapy comprising administration of FVIII;
- (4) The method according to any one of (1) to (4) above, wherein the individual has been diagnosed with mild Hemophilia;
- (5) The method according to any one of (1) to (4) above, wherein the individual has been diagnosed with moderate Hemophilia;
- (6) The method according to any one of (1) to (4) above, wherein the individual has been diagnosed with severe Hemophilia;
- (7) The method according to any one of (1) to (6) above, wherein the step of detecting the presence of the one or more SNPs comprises amplifying a nucleic acid present in the biological sample;
- (8) The method according to any one of (1) to (7) above, wherein the step of detecting the presence of the one or more SNPs comprises amplifying a nucleic acid and further (i) comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array

sequencing, and solid phase sequencing or (ii) comprises a method selected from the group consisting of a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay;

- 5 (9) The method according to any one of (1) to (8) above, wherein step (a) comprises detecting the presence of at least the following SNPs in a biological sample from the individual: T>C variant at SNP rs13206518, and at least one SNP selected from C>G variant at rs11744216, A>C variant at rs3211834, C>T variant at rs1863993, C>T variant at rs4147385, and A>C variant at rs1567748; wherein presence of the T>C variant at SNP
10 rs13206518 indicates a decreased risk of the individual developing antibodies to FVIII; presence of the C>G variant at rs11744216 indicates a decreased risk of the individual developing antibodies to FVIII; presence of the A>C variant at rs3211834 indicates a decreased risk of the individual developing antibodies to FVIII; presence of the C>T variant at rs1863993 indicates an increased risk of the individual developing antibodies to
15 FVIII; presence of the C>T variant at rs4147385 indicates an increased risk of the individual developing antibodies to FVIII; and presence of the A>C variant at rs1567748 indicates a decreased risk of the individual developing antibodies to FVIII;

- (10) The method according to any one of (1) to (9) above, wherein the method further comprises assigning a treatment to the individual based on the predicted risk of developing
20 antibodies against Factor VIII;

(11) The method of (10) above, wherein the treatment comprises administration (i) of Factor VIII, (ii) of non-Factor VIII hemostatic agent, or (iii) of Factor VIII and a non-factor VIII hemostatic agent;

- (12) The method of (10) or (11) above, wherein treatment comprising administration of
25 Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII;

(13) The method of (10) or (11) above, wherein treatment comprising Factor VIII bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII;

(14) The method of (10) or (11) above, wherein assigning treatment comprises adjusting a dosage and/or frequency of Factor VIII administration based on the predicted risk of developing antibodies against Factor VIII;

(15) The method of (14) above, wherein adjusting a dosage of Factor VIII comprises (i) increasing the dosage and/or frequency of Factor VIII administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII, or (ii) decreasing the dosage and/or frequency of Factor VIII administered to an individual with a predicted increased risk of developing antibodies against Factor VIII;

(16) The method of (10) or (11) above, wherein assigning treatment comprises adjusting a dosage and/or frequency of a non-Factor VIII hemostatic agent administration based on the predicted risk of developing antibodies against Factor VIII;

(17) The method of (16) above, wherein adjusting a dosage of a non-Factor VIII hemostatic agent comprises (i) decreasing the dosage and/or frequency of a non-Factor VIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII, or (ii) increasing the dosage and/or frequency of a non-Factor VIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies against Factor VIII;

(18) One or more oligonucleotides from 10 to 60 nucleotides in length for use in the method according to any one of (1) to (17) above, wherein the one or more oligonucleotides are capable of detecting T>C variant at SNP rs13206518;

(19) The one or more oligonucleotides according to (18) above, further comprising oligonucleotides capable of detecting at least one of the following SNPs: rs13206518, rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748;

(20) A diagnostic kit for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, moderate Hemophilia or severe Hemophilia, the kit comprising the one or more oligonucleotides according to (18) or (19) above, and a reagent for carrying out a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, and solid phase sequencing or for carrying out a method selected from the group consisting of a hybridization-based method, an enzymatic-

based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay;

- (21) The diagnostic kit according to (20) above, further comprising oligonucleotides capable of detecting at least one of the following SNPs: rs13206518, rs11744216,
5 rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748;
- (22) Use of the one or more oligonucleotides according to (18) or (19) above, for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, moderate Hemophilia or severe Hemophilia; and
- (23) The use according to (22) above, wherein the one or more oligonucleotides further
10 comprise oligonucleotides capable of detecting at least one of the following SNPs:
rs13206518, rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748.

[0018] Table 1. SNPs associated with inhibitor status in the Hemophilia Inhibitor Genetics Study (HIGS) Combined Cohort, as determined in the study described in Example 1.

5 [0019] Table 2. SNPs associated with inhibitor status in a subgroup of individuals with severe hemophilia, as determined in the study described in Example 1.

[0020] Table 3. SNPs associated with inhibitor status in the Hemophilia Inhibitor Genetics Study (HIGS) Combined Cohort, as determined in the study described in Example 2.

[0021] Table 4. SNPs associated with inhibitor status in a subgroup of individuals with severe hemophilia, as determined in the study described in Example 2.

10

DETAILED DESCRIPTION OF THE INVENTION

I. Introduction

[0022] The development of inhibitory alloantibodies against factor VIII is intricately connected with an individual's immune response to FVIII. For this reason, it has been proposed that risk factors associated with inhibitor development may include genotypes or polymorphisms associated with immune and inflammatory response. The immune response to FVIII is believed
15 to develop as an immune response to an external antigen: the antigen is recognized and processed by antigen-presenting cells (APCs) into smaller fragments, then presented on the surface of the APCs in association with major histocompatibility complex (MHC) class II molecules, where it can be recognized by CD4+ T cells specific for FVIII, which in turn, in the
20 presence of costimulatory signals, direct B cells to generate antibodies to FVIII (reviewed in Reding, *Haemophilia*, 12 (Suppl. 6):30-36 (2006)).

[0023] Several studies have found a weak association between MLC/human leukocyte antigen (HLA) class I alleles A3, B7, and C7, and MLC/HLA class II alleles DQA0102, DQB0602, DR15 and higher risk of inhibitor development, while HLA class I allele C2 and HLA class II
25 alleles DQA0103, DQB0603, and DR13 were weakly associated with a protective effect against inhibitor development (Oldenburg *et al.*, *Thromb Haemost*, 77:238-242 (1997); Hay *et al.*, *Thromb Haemost*, 77:234-237 (1997)). However, other studies, including the more recent Malmö International Brother Study (MIBS), have not found any associations between HLA genotype and inhibitor development (Lippert *et al.*, *Thromb Haemost*, 64:564-568 (1990);
30 Astermark *et al.*, *Blood*, 108:3739-3745 (2006)). Other studies have found associations between

inhibitor development and a single nucleotide polymorphism (SNP) in the promoter region of *TNFA*, encoding the immunomodulatory and pro-inflammatory cytokine tumor necrosis factor α (Astermark *et al.*, *Blood*, 108:3739-3745 (2006)); a 134 bp long variant of a CA repeat microsatellite in the promoter region of *IL10*, encoding the anti-inflammatory cytokine interleukin-10 (Astermark *et al.*, *Blood*, 107:3167-3172 (2006)); and a SNP in the promoter region of *CTLA4*, encoding cytotoxic T-lymphocyte associated protein-4, a receptor mainly displayed on activated T-cells (Astermark *et al.*, *J. Thromb. Haemost.*, 5:263-265 (2007)). However, no association was found between inhibitor development and polymorphisms in *IL1beta* and *IL4*, which encode cytokines and which have both been associated with risk of developing other autoimmune disorders (Astermark *et al.*, *Blood*, 107:3167-3172 (2006)). It is clear that other genetic markers influencing the immune response to FVIII remain to be identified. Recently, Pavlova *et al.* (Pavlova A *et al.*, *Haemophilia* 2010 May;16(102):107-12) identified a significantly higher frequency of DRB1*16 [odds ratio (OR) 10.2, 95%CI: 5.32-19.57, $P < 0.0001$] and DQB1*0502 (OR 2.2, 95%CI: 1.12-4.54, $P < 0.05$) HLA class II alleles was observed in patients with acquired hemophilia A (AH). In contrast, the frequency of DRB1*15 and DQB1*0602 alleles was found to be decreased in patients with AH corresponding to an OR of 0.4 for both HLA loci.

[0024] The present invention relates to the discovery that SNPs in multiple other immune response, immune modulator, and inflammatory response genes are associated with inhibitor development in hemophiliac patients. In the present invention, a combined cohort of three study populations, the Hemophilia Inhibitor Genetics Study (HIGS), the Malmö International Brother Study (MIBS), and the Hemophilia Growth and Development Study (HGDS), was formed to conduct an association study to test the hypothesis that antibody development to FVIII is mediated by immune response and immune modifier genes. It was discovered that out of 14,626 SNPs from 1,081 genes including cytokines and their receptors, chemokines and their receptors, pathway genes involved in inflammatory and immune responses, and HLA genes, 329 SNPs were associated with FVIII inhibitor status. The 329 SNPs of the present invention are described herein, *e.g.* in Tables 1, 2, 3, and 4. The SNPs described herein can be used to predict the risk of an individual developing antibodies to FVIII. Predicting whether an individual is at risk of developing antibodies to FVIII, whether it is prior to the individual receiving FVIII therapy or once the individual has begun receiving FVIII therapy, is important because such a prediction makes it possible to adjust the dosage and/or timing of FVIII therapy provided to the individual,

or to provide or adjust an alternative therapy such as bypass therapy, in order to avoid the individual developing antibodies to FVIII.

[0025] The present invention also relates to the discovery of strong SNP associations between inhibitor development and six markers within five genes. It was discovered that in the combined cohort, strong SNP associations with FVIII inhibitor status for the total group were observed in the *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR* genes. A strong SNP association was found for the SNP rs11744216, a C>G variant in an intronic region of the *DOCK2* gene (odds ratio or "OR" of 0.28 and a p-value or "p" of 0.00004); for the SNP rs1863993, a C>T variant in an intronic region of the *DOCK2* gene (OR 3.9, $p=0.0002$); for the SNP rs4147385, a C>T variant in an intronic region of the *MAPK9* gene (OR 2.0, $p=0.0003$); for the SNP rs13206518, a T>C variant in an intronic region of the *F13A1* gene (OR 0.32, $p=0.00007$); for the SNP rs3211834, a A>C variant in an intronic region of the *CD36* gene (OR 0.56, $p=0.0002$); and for the SNP rs1567748, a A>C variant in an intronic region of the *PTPRR* gene (OR 0.51, $p=0.0003$).

[0026] The six SNPs that were discovered to be strongly associated with inhibitor status are significant because they are located in genes that are implicated in processes of immune and/or inflammatory response and/or modulation. In some instances, the genes of the present invention are implicated in T cell development and/or T cell responsiveness. *DOCK2*, or Dedicator of cytokinesis 2, is specifically expressed in hematopoietic cells. It has been shown that *DOCK2* regulates T cell responsiveness through immunological synapse formation and that *DOCK2* is required in T cell precursors for the development of natural killer T cells, which are important for immune regulation and host defense against pathogens (Kunisaki *et al.*, *J. Immunol.*, 176:4640-4645 (2006)). *MAPK9*, also known as mitogen-activated protein kinase 9, Jun kinase 2, or stress activate protein kinase, is believed to play a key role in T cell differentiation. For example, mice deficient in *Mapk9* exhibit disruption in CD4⁺ T cell differentiation, causing selective polarization of CD4⁺ T cells to the Th2 phenotype (Jaeschke *et al.*, *Proc. Natl. Acad. Sci. USA*, 102:6931-6935 (2005); Rincón and Davis, *Immunol. Rev.*, 228:212-224 (2009)). A balance between Th1 cells (IL-1 and IFN- γ secreting cells that induce cellular immune response) and Th2 cells (IL-4, IL-5, and IL-10 secreting cells that downregulate the inflammatory activities of Th1) is critical for proper immune response, and in some autoimmune diseases there is a disruption of the Th1/Th2 balance. *PTPRR*, or protein tyrosine phosphatase receptor type R, is a signaling molecule that has been found to regulate MAP kinase activity, and therefore may also be implicated in regulating T cell differentiation by regulating *MAPK9* activity.

[0027] In some instances, the genes described herein are implicated in inflammatory response. CD36, or cluster of differentiation 36, is a class B scavenger receptor that has been shown to regulate inflammatory signaling. For example, β -amyloid, a peptide associated with Alzheimer's disease, initiates a CD36-dependent pro-inflammatory signaling cascade in mononuclear cells
5 (Moore *et al.*, *J. Biol. Chem.*, 277:47373-47379 (2002)), and CD36 is required a β -amyloid-induced CD36 upregulation of the inflammatory cytokine IL-1 β (El Khoury *et al.*, *J. Exp. Med.*, 197:1657-1666 (2003)).

[0028] In some instances, the genes described herein are implicated in the blood coagulation cascade. *F13A1* encodes coagulation factor XIII (FXIII) A subunit. Upon FXIII activation by
10 thrombin, activated FXIII acts on fibrin to form crosslinks between fibrin molecules as the final step in blood clot formation. SNPs in *F13A1* have been reported to be associated with other aspects blood coagulation, specifically plasma fibrinogen concentration and fibrin clot porosity (Mannila *et al.*, *Thromb. Haemost.*, 95:420-427 (2006)).

[0029] The present invention also relates to the discovery of strong SNP associations between
15 inhibitor development in patients with severe hemophilia and four markers within three genes. It was discovered that in the combined cohort, strong SNP associations with FVIII inhibitor status for the subgroup with severe hemophilia were observed in the *DOCK2*, *MAPK9*, and *CD36* genes. For this subgroup, a strong association with inhibitor development was found for the SNP rs4147385, a C>T variant in an intronic region of the *MAPK9* gene (OR 2.3, $p=0.00003$); for the
20 SNP rs11744216, a C>G variant in an intronic region of the *DOCK2* gene (OR 0.30, $p=0.00008$); for the SNP rs1863993, a C>T variant in an intronic region of the *DOCK2* gene (OR 4.4, $p=0.0009$); and for the SNP rs3211834, a A>C variant in an intronic region of the *CD36* gene (OR 0.59, $p=0.0008$).

[0030] In one aspect, the present invention provides a method for predicting the risk of an
25 individual developing antibodies to factor VIII (FVIII), the method comprising the steps of identifying at least one single nucleotide polymorphism (SNP) selected from the group consisting of the SNPs listed in Table 1, and predicting the risk of the individual of developing antibodies to FVIII.

[0031] In one embodiment, the SNP is located in a gene selected from the group consisting of
30 *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR*. In one embodiment, the SNP is selected from the group consisting of rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748.

[0032] In one embodiment, the method further comprises the steps of amplifying genomic DNA of the individual using oligonucleotide primers that amplify the SNP selected from the group consisting of the SNPs listed in Table 1, and identifying the nucleotides present at the SNP.

5 [0033] In one embodiment, the individual has not yet received FVIII therapy. In one embodiment, the individual has received FVIII therapy. In one embodiment, the prediction allows for adjusting a dosage of FVIII therapy received by the individual. In one embodiment, the prediction allows for providing or adjusting a dosage of bypass therapy received by the individual.

10 [0034] In one embodiment, the individual has severe hemophilia. In one embodiment, the individual has severe hemophilia and the SNP is located in a gene selected from the group consisting of *DOCK2*, *MAPK9*, and *CD36*. In one embodiment, the individual has severe hemophilia and the SNP is selected from the group consisting of rs11744216, rs1863993, rs4147385, and rs3211834.

15 [0035] In one embodiment, the method further comprises the steps of analyzing a sample from the individual with an assay that specifically detects the SNP selected from the group consisting of the SNPs listed in Table 1, and identifying the nucleotides present at the SNP. In one embodiment, the assay or step of identification comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal
20 cycle sequencing, capillary array sequencing, and solid phase sequencing. In one embodiment, the assay comprises microarray hybridization.

[0036] In another aspect, the present invention provides an oligonucleotide from 10 to 60 nucleotides in length that contacts at least one single nucleotide polymorphism (SNP) selected from the group consisting of the SNPs listed in Table 1. In one embodiment, the oligonucleotide
25 contacts a SNP located in a gene selected from the group consisting of *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR*. In one embodiment, the oligonucleotide contacts a SNP selected from the group consisting of rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748. In one embodiment, the oligonucleotide is used to predict the risk of an individual developing antibodies to factor VIII (FVIII) and to adjust a dosage of FVIII therapy received by the
30 individual. In one embodiment, the oligonucleotide is used to provide or adjust a dosage of bypass therapy received by the individual.

[0037] In another aspect, the present invention provides a diagnostic kit comprising oligonucleotides to detect at least one single nucleotide polymorphism (SNP) selected from the group consisting of the SNPs listed in Table 1. In one embodiment, the kit comprises oligonucleotides that detect a SNP located in a gene selected from the group consisting of

5 *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR*. In one embodiment, the kit comprises oligonucleotides that detect a SNP selected from the group consisting of rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748. In one embodiment, the kit is used to predict the risk of an individual developing antibodies to factor VIII (FVIII) and to adjust a dosage of FVIII therapy received by the individual. In one embodiment, the kit is used to

10 provide or adjust a dosage of bypass therapy received by the individual.

[0038] In yet another aspect, the present invention provides a microarray comprising a support having a plurality of discrete regions, each discrete region having a nucleic acid fragment spotted thereon, wherein the nucleic acid fragment comprises a sequence that is complementary to a single nucleotide polymorphism (SNP) selected from the group consisting of the SNPs listed in

15 Table 1. In one embodiment, the microarray is used to predict the risk of an individual developing antibodies to factor VIII (FVIII) and to adjust a dosage of FVIII therapy received by the individual. In one embodiment, the microarray is used to provide or adjust a dosage of bypass therapy received by the individual.

[0039] In still another aspect, the present invention provides an isolated nucleic acid

20 comprising a single nucleotide polymorphism (SNP) selected from the group consisting of the SNPs listed in Table 1. In one embodiment, the SNP is located in a gene selected from the group consisting of *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR*. In one embodiment, the SNP is selected from the group consisting of rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748.

25 [0040] The present invention may be understood more readily by reference to the following detailed description of specific embodiments and the Examples included therein.

II. Definitions

[0041] As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

- [0042] As used herein, the term "factor VIII" or "FVIII" refers to any form of factor VIII molecule with the typical characteristics of blood coagulation factor VIII, whether derived from blood plasma or produced through the use of recombinant DNA techniques, and including all modified forms of factor VIII. Factor VIII (FVIII) exists naturally and in therapeutic preparations as a heterogeneous distribution of polypeptides arising from a single gene product (see, e.g., Andersson et al., *Proc. Natl. Acad. Sci. USA*, 83:2979-2983 (1986)). Commercially available examples of therapeutic preparations containing Factor VIII include those sold under the trade names of HEMOFIL M, ADVATE, and RECOMBINATE (available from Baxter Healthcare Corporation, Deerfield, Ill., U.S.A.).
- 10 [0043] As used herein, the term "inhibitory antibodies to factor VIII" refers to antibodies that decrease or neutralize the procoagulant function of factor VIII. Inhibitory antibodies to factor VIII may develop in individuals who are not hemophiliacs, or they may develop in individuals with mild, moderate, or severe hemophilia. An individual may develop inhibitory antibodies to factor VIII prior to receiving any factor VIII therapy, or an individual may develop inhibitory antibodies to factor VIII after the onset of factor VIII therapy. In an individual receiving factor VIII therapy, inhibitory antibodies to factor VIII often appear early in the course of therapy, typically after about 9 to 11 exposure days, but sometimes develop sooner or later than 9 to 11 exposure days, within about 100 exposure days, and may develop at any time after the onset of factor VIII therapy.
- 20 [0044] As used herein, the term "single nucleotide polymorphism" or "SNP" refers to the occurrence of two or more genetically determined alternative genotypes in a population. A SNP can occur in a coding (*i.e.* gene) region of the genome, including the promoter region, untranslated 5' and 3' regions, introns, and coding regions found in the mRNA, or alternatively can occur in a noncoding region of the genome. In some embodiments, the SNPs associated with gene sequences of the invention may be located within 300,000; 200,000; 100,000; 75,000; 25 50,000; or 10,000 base pairs from the gene sequence. SNP analysis is useful for detecting differences between polynucleotide sequences, such as the sequences identified in Table 1, that are associated with increased risk of developing a disease or condition, such as developing inhibitory antibodies to FVIII. These polynucleotide sequences may occur in or near any of the genes listed in Table 1, including for example *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR*. 30 The SNPs of the present invention are useful, for instance, for predicting the risk of developing inhibitory antibodies to FVIII. For example, if an individual carries at least one SNP linked to a

disease-associated allele of the gene sequences of the invention, the individual is likely at increased risk for developing inhibitory antibodies to FVIII.

[0045] It will be understood by the skilled artisan that SNPs may be used singly or in combination with other SNPs for any of the uses, *e.g.*, predicting the risk of developing inhibitory antibodies to FVIII, disclosed herein.

[0046] As used herein, the term "gene" refers to the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding region, such as the promoter and 3'-untranslated region, respectively, as well as intervening sequences (introns) between individual coding segments (exons).

10 [0047] As used herein, the term "oligonucleotide" refers to a nucleic acid sequence of approximately 5 nucleotides or greater in length, and up to as many as approximately 100 nucleotides in length, which can be used as a primer, probe, or amplimer. Oligonucleotides are often between about 10 and about 50 nucleotides in length, more often between about 10 and about 40 nucleotides, very often between about 15 and about 30 nucleotides, and the terms
15 oligonucleotides or oligomers can also refer to synthetic and/or non-naturally occurring nucleic acids (*i.e.*, comprising nucleic acid analogues or modified backbone residues or linkages)

[0048] As used herein, the term "nucleic acid" refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form, and complements thereof. The term encompasses nucleic acids containing known nucleotide analogs or modified
20 backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides, and peptide-nucleic acids (PNAs).

25 [0049] For PCR, a temperature of about 36°C is typical for low stringency amplification, although annealing temperatures may vary between about 32°C and 48°C depending on primer length. For high stringency PCR amplification, a temperature of about 62°C is typical, although high stringency annealing temperatures can range from about 50°C to about 65°C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency
30 amplifications include a denaturation phase of 90°C - 95°C for 30 sec - 2 min., an annealing phase lasting 30 sec. - 2 min., and an extension phase of about 72°C for 1 - 2 min. Protocols and

guidelines for low and high stringency amplification reactions are provided, e.g., in Innis *et al.* (1990) *PCR Protocols, A Guide to Methods and Applications*, Academic Press, Inc. N.Y.). ash conditions can be utilized to provide conditions of similar stringency.

[0050] As used herein, the term "sample" includes extractions of nucleic acid such as DNA, sections of tissues such as biopsy and autopsy samples, and frozen sections taken for histological purposes. Such samples include blood and blood fractions or products (e.g., serum, buffy coat, plasma, platelets, red blood cells, and the like), sputum, cheek cells tissue, cultured cells (e.g., primary cultures, explants, and transformed cells), stool, urine, other biological fluids (e.g., prostatic fluid, gastric fluid, intestinal fluid, renal fluid, lung fluid, cerebrospinal fluid, and the like), *etc.* A sample is typically obtained from a "subject" such as a eukaryotic organism, most preferably a mammal such as a primate, e.g., chimpanzee or human; cow; dog; cat; a rodent, e.g., guinea pig, rat, mouse; rabbit; or a bird; reptile; or fish.

[0051] As used herein, the terms "hemophilia" or "haemophilia" refer to a group of disease states broadly characterized by reduced blood clotting or coagulation. Hemophilia may refer to Type A, Type B, or Type C hemophilia, or to the composite of all three diseases types. Type A hemophilia (hemophilia A) is caused by a reduction or loss of factor VIII (FVIII) activity and is the most prominent of the hemophilia subtypes. Type B hemophilia (hemophilia B) results from the loss or reduction of factor IX (FIX) clotting function. Type C hemophilia (hemophilia C) is a consequence of the loss or reduction in factor XI (FXI) clotting activity. Hemophilia A and B are X-linked diseases, while hemophilia C is autosomal. Common treatments for hemophilia include both prophylactic and on-demand administration of clotting factors, such as FVIII, FIX, including Bebulin®-VH, and FXI, as well as FEIBA-VH, desmopressin, and plasma infusions.

[0052] As used herein, the term "FVIII therapy" includes any therapeutic approach of providing factor VIII to a patient to relieve, diminish, or prevent the reoccurrence of one or more symptoms (*i.e.*, clinical factors) associated with hemophilia. The term encompasses administering any compound, drug, procedure, or regimen comprising factor VIII, including any modified form of factor VIII, which is useful for maintaining or improving the health of an individual with hemophilia and includes any of the therapeutic agents described herein. One skilled in the art will appreciate that either the course of FVIII therapy or the dose of FVIII therapy can be changed, e.g., based upon the results obtained in accordance with the present invention.

[0053] As used herein, the term "bypass therapy" includes any therapeutic approach of providing non-factor VIII hemostatic agents, compounds or coagulation factors to a patient to relieve, diminish, or prevent the reoccurrence of one or more symptoms (*i.e.*, clinical factors) associated with hemophilia. Non-FVIII compounds and coagulation factors that may be provided include, but are not limited to, Factor VIII Inhibitor Bypass Activity (FEIBA), recombinant activated factor VII (FVIIa), prothrombin complex concentrates, and activated prothrombin complex concentrates. These non-FVIII compounds and coagulation factors may be recombinant or plasma-derived. One skilled in the art will appreciate that either the course of bypass therapy or the dose of bypass therapy can be changed, *e.g.*, based upon the results obtained in accordance with the present invention.

[0054] As used herein, a "combination therapy comprising administration of FVIII and a FVIII bypass agent" includes any therapeutic approach of providing both Factor VIII and a non-Factor VIII hemostatic agent to a patient to relieve, diminish, or prevent the reoccurrence of one or more symptoms (*i.e.*, clinical factors) associated with hemophilia. The term encompasses administering any compound, drug, procedure, or regimen comprising factor VIII, including any modified form of factor VIII, which is useful for maintaining or improving the health of an individual with hemophilia and includes any of the therapeutic agents described herein. Non-FVIII compounds and coagulation factors that may be provided include, but are not limited to, Factor VIII Inhibitor Bypass Activity (FEIBA), recombinant activated factor VII (FVIIa), prothrombin complex concentrates, and activated prothrombin complex concentrates. The Factor VIII and non-Factor VIII compounds and coagulation factors may be recombinant or plasma-derived.

[0055] In one embodiment, combination therapy may refer to administration of Factor VIII and a non-FVIII hemostatic agent in a single therapeutic dose. In another embodiment, combination therapy may refer to administration of Factor VIII and a non-FVIII hemostatic agent in separate therapeutic doses. For example, Factor VIII and a non-FVIII hemostatic agent may be administered in separate doses received according to a single dosage schedule, or alternatively in separate doses received according to separate dosing schedules. In one embodiment, the dosing schedules for the Factor VIII and the non-FVIII hemostatic agent may be concurrent or alternating (*i.e.*, overlapping). In another embodiment, the dosing schedules may be non-overlapping (*i.e.*, where one dosing regime is completed before beginning a second dosing regime with the alternate therapy). One skilled in the art will appreciate that either the course

and/or dose of FVIII therapy and/or non-FVIII hemostatic agent (*i.e.*, FVIII bypass agent) can be changed, *e.g.*, based upon the results obtained in accordance with the present invention. In one embodiment, the identification of SNPs corresponding to one or more SNPs found in Tables 1 to 4, in a sample from a patient diagnosed with Hemophilia, will allow one of skill in the art to
5 tailor the combination therapy (*i.e.*, increase or decrease the regime and/or dose of one or both of the Factor VIII and FVIII bypass agent) to the individual, based on the individuals risk of developing Factor VIII inhibitors.

[0056] The terms "therapeutically effective amount or dose" or "therapeutically sufficient amount or dose" or "effective or sufficient amount or dose" refer to a dose that produces
10 therapeutic effects for which it is administered. For example, a therapeutically effective amount of a drug useful for treating hemophilia can be the amount that is capable of preventing or relieving one or more symptoms associated with hemophilia. The exact dose will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (*see, e.g.*, Lieberman, *Pharmaceutical Dosage Forms* (vols. 1-3, 1992); Lloyd, *The*
15 *Art, Science and Technology of Pharmaceutical Compounding* (1999); Pickar, *Dosage Calculations* (1999); and *Remington: The Science and Practice of Pharmacy*, 20th Edition, 2003, Gennaro, Ed., Lippincott, Williams & Wilkins).

[0057] As used herein, an "increased risk" of developing antibodies against Factor VIII refers to an increased probability or increased likelihood that an individual will develop antibodies
20 against Factor VIII, for example, in response to treatment comprising administration of Factor VIII. In one embodiment, the increased risk is in comparison with an average risk of developing Factor VIII inhibitors in a given Hemophilia A population (*e.g.*, the average risk ascribed to an individual for which SNP genotyping has not been performed. In certain embodiments, an increased risk will correspond to at least a 5% increased risk. In another embodiment, an
25 increased risk will correspond to at least a 10% increased risk. In another embodiment, an increased risk will correspond to at least a 25% increased risk. In another embodiment, an increased risk will correspond to at least a 50% increased risk. In another embodiment, an increased risk will correspond to at least a 75% increased risk. In another embodiment, an increased risk will correspond to at least a 100% increased risk. In another embodiment, an
30 increased risk will correspond to at least a 150% increased risk. In another embodiment, an increased risk will correspond to at least a 200% increased risk. In another embodiment, an increased risk will correspond to at least a 250% increased risk. In another embodiment, an

increased risk will correspond to at least a 300% increased risk. In yet other embodiments, an increased risk will correspond to at least a 5% increased risk, or at least a 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, 200%, 210%, 220%, 230%, 240%,
5 250%, 260%, 270%, 280%, 290%, 300%, 310%, 320%, 330%, 340%, 350%, 360%, 370%, 380%, 390%, 400%, 410%, 420%, 430%, 440%, 450%, 460%, 470%, 480%, 490%, 500%, 525%, 550%, 575%, 600%, 625%, 650%, 675%, 700%, 750%, 800%, 850%, 900%, 950%, 1000%, or greater increased risk.

[0058] As used herein, a “decreased risk” of developing antibodies against Factor VIII refers
10 to a decreased probability or decreased likelihood that a individual will develop antibodies against Factor VIII, for example, in response to treatment comprising administration of Factor VIII. In one embodiment, the decreased risk is in comparison with a average risk of developing Factor VIII inhibitors in a given Hemophilia A population (*e.g.*, the average risk ascribed to a individual for which SNP genotyping has not been performed). In certain embodiments, a
15 decreased risk will correspond to at least a 5% decreased risk. In another embodiment, a decreased risk will correspond to at least a 10% decreased risk. In another embodiment, a decreased risk will correspond to at least a 25% decreased risk. In another embodiment, a decreased risk will correspond to at least a 50% decreased risk. In another embodiment, a decreased risk will correspond to at least a 75% decreased risk. In another embodiment, a
20 decreased risk will correspond to at least a 100% decreased risk. In another embodiment, a decreased risk will correspond to at least a 150% decreased risk. In another embodiment, a decreased risk will correspond to at least a 200% decreased risk. In another embodiment, a decreased risk will correspond to at least a 250% decreased risk. In another embodiment, a decreased risk will correspond to at least a 300% decreased risk. In yet other embodiments, a
25 decreased risk will correspond to at least a 5% decreased risk, or at least a 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, 200%, 210%, 220%, 230%, 240%, 250%, 260%, 270%, 280%, 290%, 300%, 310%, 320%, 330%, 340%, 350%, 360%, 370%, 380%, 390%, 400%, 410%, 420%, 430%, 440%, 450%, 460%, 470%, 480%, 490%, 500%,
30 525%, 550%, 575%, 600%, 625%, 650%, 675%, 700%, 750%, 800%, 850%, 900%, 950%, 1000%, or greater decreased risk.

III. Predictive Methods and Assays

[0059] In certain aspects, the present invention provides methods for predicting the risk of an individual developing antibodies to factor VIII (FVIII). Risk prediction involves identifying at least one single nucleotide polymorphism (SNP) selected from the group consisting of the SNPs listed in Table 1, and on the basis of the nucleotides present at the SNP, determining whether the individual is more likely to develop antibodies to FVIII or not. SNP analysis is useful for detecting differences between alleles of the polynucleotides (*e.g.*, genes) of the invention. For example, if an individual carries at least one SNP linked to a disease or condition-associated allele of the gene sequences of the invention, the individual is likely at an increased risk of developing antibodies to FVIII. In some embodiments, the SNP associated with the gene sequences of the invention is located within 300,000; 200,000; 100,000; 75,000; 50,000; or 10,000 base pairs from the gene sequence.

[0060] Predicting the risk of an individual developing antibodies to FVIII may be performed when the individual has not received any FVIII therapy. Alternatively, risk prediction may be performed soon after the individual begins receiving FVIII therapy. Alternatively, risk prediction may be performed at any time when there are suspected symptoms of FVIII antibody development in the individual. One of skill in the art will be able to identify symptoms of FVIII antibody development in the individual.

[0061] In some embodiments, the present invention provides methods of predicting the risk of an individual developing antibodies to FVIII comprising identifying a SNP located in a gene selected from the group consisting of *DOCK2*, *MAPK9*, *F13A1*, *CD36*, and *PTPRR*. In one embodiment, the method comprises identifying the SNP rs11744216 and determining whether the individual has a C>G polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the method comprises identifying the SNP rs13206518 and determining whether the individual has a T>C polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the method comprises identifying the SNP rs3211834 and determining whether the individual has a A>C polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the method comprises identifying the SNP rs1863993 and determining whether the individual has a C>T polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the method comprises identifying the SNP rs4147385

and determining whether the individual has a C>T polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the method comprises identifying the SNP rs1567748 and determining whether the individual has a A>C polymorphism that is associated with increased risk of developing antibodies to FVIII.

5 [0062] The predictive methods of the present invention may also be used to determine how to provide or adjust a dosage of therapy received by the individual. In some embodiments, the identification of a variant or condition-associated genotype for a SNP selected from the SNPs listed in Table 1 allows for adjusting a dosage of FVIII therapy received by the individual. In some embodiments, the identification of a variant or condition-associated genotype for a SNP
10 selected from the SNPs listed in Table 1 allows for providing or adjusting a dosage of bypass therapy received by the individual.

[0063] In some embodiments of the present invention, the individual for whom the risk prediction is desired may be an individual who has severe hemophilia. In some embodiments wherein the individual for whom the risk prediction is desired has severe hemophilia, the SNP to
15 be identified may be located in a gene selected from the group consisting of *DOCK2*, *MAPK9*, and *CD36* (Table 2). In one embodiment, the individual has severe hemophilia and the method comprises identifying the SNP rs11744216 and determining whether the individual has a C>G polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the individual has severe hemophilia and the method comprises identifying the
20 SNP rs1863993 and determining whether the individual has a C>T polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the individual has severe hemophilia and the method comprises identifying the SNP rs4147385 and determining whether the individual has a C>T polymorphism that is associated with increased risk of developing antibodies to FVIII. In one embodiment, the individual has severe hemophilia
25 and the method comprises identifying the SNP rs3211834 and determining whether the individual has a A>C polymorphism that is associated with increased risk of developing antibodies to FVIII.

[0064] The genotype of the SNP of interest in the individual may be measured by taking a blood, saliva, urine, or other tissue sample containing nucleic acid, e.g., DNA, from the
30 individual and analyzing the sample with an assay that specifically detects the presence of the SNP of interest. Alternatively, the genotype of the SNP of interest in the individual may be

measured by taking a blood, saliva, urine, or other tissue sample from the individual and amplifying the genomic DNA of the sample using oligonucleotide primers that amplify the SNP of interest.

A. Methods for Predicting Risk in Hemophilia Patients

5 [0065] In one aspect, the present invention provides methods for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia A by detecting the presence of one or more of the SNPs identified herein. In one embodiment, the method comprises the steps of detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed
10 in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0066] Generally, the predicted risk associated with each SNP is relative to the Odds ratio (OR) calculated for that particular SNP. Therefore, the detection of a SNP with an OR less than one is generally associated with a reduced likelihood (i.e., a reduced risk) of the individual
15 developing antibodies against Factor VIII. Likewise, the detection of a SNP with an OR greater than one is generally associated with an increased likelihood (i.e., a reduced risk) of the individual developing antibodies against Factor VIII. Accordingly, treatment can then be assigned and/or administered to an individual diagnosed with Hemophilia A appropriately based on the relative risk of the individual developing antibodies against Factor VIII.

20 1. Individuals Diagnosed with Hemophilia A

[0067] In one embodiment, the present invention provides a method for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia A the method comprising the steps of detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed
25 in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0068] In one embodiment of the method, the individual has been diagnosed with mild Hemophilia. In another embodiment, the individual has been diagnosed with moderate Hemophilia. In yet another embodiment, the individual has been diagnosed with severe
30 Hemophilia.

[0069] In one embodiment of the method, the step of detecting the presence of at least one SNP comprises amplifying a nucleic acid present in the biological sample. In another embodiment, the step of detecting the presence of at least one SNP comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, solid phase sequencing, a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.

[0070] In one embodiment, the method further comprises assigning and/or administering a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, treatment comprising administration of Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0071] In yet another specific embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is assigned to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0072] In one embodiment, treatment comprising administration of Factor VIII is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0073] In yet another embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is provided to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0074] In one embodiment, the method further comprises adjusting a dosage of a treatment comprising administration of Factor VIII to the individual based on the predicted risk of

developing antibodies against Factor VIII. In a specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII is increased. In another specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted increased risk of developing antibodies against Factor VIII is decreased.

[0075] In another embodiment, the method further comprises adjusting the dosage and/or frequency of Factor VIII administration in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0076] In another embodiment, the method further comprises adjusting the dosage and/or frequency of a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0077] In another embodiment, the method further comprises adjusting the dosage and/or frequency of both Factor VIII and a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In this fashion, a combination therapy may be optimized for an individual with a specific predicted risk of developing antibodies against FVIII. Optimization of the dosage and/or frequency of Factor VIII and non-FVIII hemostatic agents in combination therapy may be achieved by any combination of increasing the frequency of FVIII administration, decreasing the frequency of FVIII administration, increasing the dosage of FVIII, decreasing the dosage of FVIII, increasing the frequency of non-FVIII hemostatic agent administration, decreasing the frequency of non-FVIII

hemostatic agent administration, increasing the dosage of a non-FVIII hemostatic agent, and decreasing the dosage of a non-FVIII hemostatic agent.

[0078] In a specific embodiment, the method comprises increasing the frequency and/or dosage of FVIII and decreasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0079] In another specific embodiment, the method comprises decreasing the frequency and/or dosage of FVIII and increasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0080] In a preferred embodiment, the method comprises the detection of at least one SNP selected from those listed in Table 3. In a specific embodiment, the method comprises the detection of at least one SNP selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712. In one embodiment, at least one detected SNP is rs12368829. In another embodiment, at least one detected SNP is rs11744216. In another embodiment, at least one detected SNP is rs1863993. In another embodiment, at least one detected SNP is rs4147385. In another embodiment, at least one detected SNP is rs12546235. In another embodiment, at least one detected SNP is rs4242389. In another embodiment, at least one detected SNP is rs10054825. In another embodiment, at least one detected SNP is rs17535213. In another embodiment, at least one detected SNP is rs10072056. In another embodiment, at least one detected SNP is rs17725712.

a) Prior to Factor VIII Therapy

[0081] In one embodiment, the present invention relates specifically to an individual or group of individuals diagnosed with Hemophilia A that have not previously received Factor VIII therapy (*i.e.*, not received treatment comprising administration of Factor VIII).

[0082] In one embodiment, a method is provided for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia A, who has not previously received treatment comprising administration of FVIII, comprising detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group

consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0083] In one embodiment of the method, the individual has been diagnosed with mild Hemophilia. In another embodiment, the individual has been diagnosed with moderate Hemophilia. In yet another embodiment, the individual has been diagnosed with severe Hemophilia.

[0084] In one embodiment of the method, the step of detecting the presence of at least one SNP comprises amplifying a nucleic acid present in the biological sample. In another embodiment, the step of detecting the presence of at least one SNP comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, solid phase sequencing, a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.

[0085] In one embodiment, the method further comprises assigning and/or administering a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, treatment comprising administration of Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0086] In yet another specific embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is assigned to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0087] In one embodiment, treatment comprising administration of Factor VIII is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0088] In yet another embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is provided to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0089] In one embodiment, the method further comprises adjusting a dosage of a treatment comprising administration of Factor VIII to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII is increased. In another specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted increased risk of developing antibodies against Factor VIII is decreased.

[0090] In another embodiment, the method further comprises adjusting the dosage and/or frequency of Factor VIII administration in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0091] In another embodiment, the method further comprises adjusting the dosage and/or frequency of a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0092] In another embodiment, the method further comprises adjusting the dosage and/or frequency of both Factor VIII and a non-FVIII hemostatic agent administered in a combination

- therapy based on the predicted risk of developing antibodies against FVIII. In this fashion, a combination therapy may be optimized for an individual with a specific predicted risk of developing antibodies against FVIII. Optimization of the dosage and/or frequency of Factor VIII and non-FVIII hemostatic agents in combination therapy may be achieved by any combination of
- 5 increasing the frequency of FVIII administration, decreasing the frequency of FVIII administration, increasing the dosage of FVIII, decreasing the dosage of FVIII, increasing the frequency of non-FVIII hemostatic agent administration, decreasing the frequency of non-FVIII hemostatic agent administration, increasing the dosage of a non-FVIII hemostatic agent, and decreasing the dosage of a non-FVIII hemostatic agent.
- 10 **[0093]** In a specific embodiment, the method comprises increasing the frequency and/or dosage of FVIII and decreasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII.
- [0094]** In another specific embodiment, the method comprises decreasing the frequency and/or
- 15 dosage of FVIII and increasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.
- [0095]** In a preferred embodiment, the method comprises the detection of at least one SNP selected from those listed in Table 3. In a specific embodiment, the method comprises the
- 20 detection of at least one SNP selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712. In one embodiment, at least one detected SNP is rs12368829. In another embodiment, at least one detected SNP is rs11744216. In another embodiment, at least one detected SNP is rs1863993. In another embodiment, at least one detected SNP is rs4147385. In
- 25 another embodiment, at least one detected SNP is rs12546235. In another embodiment, at least one detected SNP is rs4242389. In another embodiment, at least one detected SNP is rs10054825. In another embodiment, at least one detected SNP is rs17535213. In another embodiment, at least one detected SNP is rs10072056. In another embodiment, at least one detected SNP is rs17725712.

b) After Initial Factor VIII Therapy

[0096] In one embodiment, the present invention relates specifically to an individual or group of individuals diagnosed with Hemophilia A that have previously received Factor VIII therapy (*i.e.*, received treatment comprising administration of Factor VIII).

5 **[0097]** In one embodiment, a method is provided for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia A, who has previously received treatment comprising administration of FVIII, comprising detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 1, a SNP listed in Table 2, a SNP listed in Table 3, and a SNP
10 listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0098] In one embodiment of the method, the individual has been diagnosed with mild Hemophilia. In another embodiment, the individual has been diagnosed with moderate Hemophilia. In yet another embodiment, the individual has been diagnosed with severe
15 Hemophilia.

[0099] In one embodiment of the method, the step of detecting the presence of at least one SNP comprises amplifying a nucleic acid present in the biological sample. In another embodiment, the step of detecting the presence of at least one SNP comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, solid phase sequencing, a
20 hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.

[0100] In one embodiment, the method further comprises assigning and/or administering a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, treatment comprising administration of Factor VIII is assigned
25 to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0101] In yet another specific embodiment, combination therapy comprising administration of
30 Factor VIII and a FVIII bypass agent is assigned to an individual based on the predicted risk of

developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

5 [0102] In one embodiment, treatment comprising administration of Factor VIII is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0103] In yet another embodiment, combination therapy comprising administration of Factor
10 VIII and a FVIII bypass agent is provided to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

15 [0104] In one embodiment, the method further comprises adjusting a dosage of a treatment comprising administration of Factor VIII to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII is increased. In another specific embodiment, a dosage of Factor VIII to be
20 administered to an individual with a predicted increased risk of developing antibodies against Factor VIII is decreased.

[0105] In another embodiment, the method further comprises adjusting the dosage and/or frequency of Factor VIII administration in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the
25 dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII.

30 [0106] In another embodiment, the method further comprises adjusting the dosage and/or frequency of a non-FVIII hemostatic agent administered in a combination therapy based on the

predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0107] In another embodiment, the method further comprises adjusting the dosage and/or frequency of both Factor VIII and a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In this fashion, a combination therapy may be optimized for an individual with a specific predicted risk of developing antibodies against FVIII. Optimization of the dosage and/or frequency of Factor VIII and non-FVIII hemostatic agents in combination therapy may be achieved by any combination of increasing the frequency of FVIII administration, decreasing the frequency of FVIII administration, increasing the dosage of FVIII, decreasing the dosage of FVIII, increasing the frequency of non-FVIII hemostatic agent administration, decreasing the frequency of non-FVIII hemostatic agent administration, increasing the dosage of a non-FVIII hemostatic agent, and decreasing the dosage of a non-FVIII hemostatic agent.

[0108] In a specific embodiment, the method comprises increasing the frequency and/or dosage of FVIII and decreasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0109] In another specific embodiment, the method comprises decreasing the frequency and/or dosage of FVIII and increasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0110] In a preferred embodiment, the method comprises the detection of at least one SNP selected from those listed in Table 3. In a specific embodiment, the method comprises the detection of at least one SNP selected from the group consisting of rs12368829, rs11744216, rs1863993, rs4147385, rs12546235, rs4242389, rs10054825, rs17535213, rs10072056, and rs17725712. In one embodiment, at least one detected SNP is rs12368829. In another embodiment, at least one detected SNP is rs11744216. In another embodiment, at least one

detected SNP is rs1863993. In another embodiment, at least one detected SNP is rs4147385. In another embodiment, at least one detected SNP is rs12546235. In another embodiment, at least one detected SNP is rs4242389. In another embodiment, at least one detected SNP is rs10054825. In another embodiment, at least one detected SNP is rs17535213. In another
5 embodiment, at least one detected SNP is rs10072056. In another embodiment, at least one detected SNP is rs17725712.

2. Individuals Diagnosed with Severe Hemophilia A

[0111] In one embodiment, the present invention provides a method for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with severe
10 Hemophilia A, the method comprising the steps of detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0112] In one embodiment of the method, the step of detecting the presence of at least one
15 SNP comprises amplifying a nucleic acid present in the biological sample. In another embodiment, the step of detecting the presence of at least one SNP comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, solid phase sequencing, a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing
20 method, a ssDNA conformational method, and a DNA melting temperature assay.

[0113] In one embodiment, the method further comprises assigning and/or administering a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, treatment comprising administration of Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In
25 another specific embodiment, treatment comprising Factor VIII bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0114] In yet another specific embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is assigned to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is
30 assigned to an individual with a predicted decreased risk of developing antibodies against Factor

VIII. In another specific embodiment, a combination therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0115] In one embodiment, treatment comprising administration of Factor VIII is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0116] In yet another embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is provided to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0117] In one embodiment, the method further comprises adjusting a dosage of a treatment comprising administration of Factor VIII to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII is increased. In another specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted increased risk of developing antibodies against Factor VIII is decreased.

[0118] In another embodiment, the method further comprises adjusting the dosage and/or frequency of Factor VIII administration in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0119] In another embodiment, the method further comprises adjusting the dosage and/or frequency of a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of a non-FVIII hemostatic agent administered in a

combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

5 [0120] In another embodiment, the method further comprises adjusting the dosage and/or frequency of both Factor VIII and a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In this fashion, a combination therapy may be optimized for an individual with a specific predicted risk of developing antibodies against FVIII. Optimization of the dosage and/or frequency of Factor VIII
10 and non-FVIII hemostatic agents in combination therapy may be achieved by any combination of increasing the frequency of FVIII administration, decreasing the frequency of FVIII administration, increasing the dosage of FVIII, decreasing the dosage of FVIII, increasing the frequency of non-FVIII hemostatic agent administration, decreasing the frequency of non-FVIII hemostatic agent administration, increasing the dosage of a non-FVIII hemostatic agent, and
15 decreasing the dosage of a non-FVIII hemostatic agent.

[0121] In a specific embodiment, the method comprises increasing the frequency and/or dosage of FVIII and decreasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

20 [0122] In another specific embodiment, the method comprises decreasing the frequency and/or dosage of FVIII and increasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0123] In a preferred embodiment, the method comprises the detection of at least one SNP
25 selected from those listed in Table 4. In a specific embodiment, the method comprises the detection of at least one SNP selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888. In one embodiment, at least one detected SNP is rs12368829. In another embodiment, at least one detected SNP is
30 rs4147385. In another embodiment, at least one detected SNP is rs11744216. In another embodiment, at least one detected SNP is rs1863993. In another embodiment, at least one

detected SNP is rs17535213. In another embodiment, at least one detected SNP is rs10072056. In another embodiment, at least one detected SNP is rs10054825. In another embodiment, at least one detected SNP is rs12546235. In another embodiment, at least one detected SNP is rs4242389. In another embodiment, at least one detected SNP is rs2071336. In another
5 embodiment, at least one detected SNP is rs414634. In another embodiment, at least one detected SNP is rs17725712. In another embodiment, at least one detected SNP is rs11773821. In another embodiment, at least one detected SNP is rs8005905. In another embodiment, at least one detected SNP is rs9482888.

a) Prior to Factor VIII Therapy

10 **[0124]** In one embodiment, the present invention relates specifically to an individual or group of individuals diagnosed with severe Hemophilia A that have not previously received Factor VIII therapy (*i.e.*, not received treatment comprising administration of Factor VIII).

[0125] In one embodiment, a method is provided for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with severe Hemophilia A, who
15 has not previously received treatment comprising administration of FVIII, comprising detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0126] In one embodiment of the method, the individual has been diagnosed with mild
20 Hemophilia. In another embodiment, the individual has been diagnosed with moderate Hemophilia. In yet another embodiment, the individual has been diagnosed with severe Hemophilia.

[0127] In one embodiment of the method, the step of detecting the presence of at least one SNP comprises amplifying a nucleic acid present in the biological sample. In another
25 embodiment, the step of detecting the presence of at least one SNP comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, solid phase sequencing, a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.

[0128] In one embodiment, the method further comprises assigning and/or administering a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, treatment comprising administration of Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In
5 another specific embodiment, treatment comprising Factor VIII bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0129] In yet another specific embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is assigned to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is
10 assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0130] In one embodiment, treatment comprising administration of Factor VIII is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In
15 another specific embodiment, treatment comprising Factor VIII bypass therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0131] In yet another embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is provided to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is
20 provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, a combination therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0132] In one embodiment, the method further comprises adjusting a dosage of a treatment comprising administration of Factor VIII to the individual based on the predicted risk of
25 developing antibodies against Factor VIII. In a specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII is increased. In another specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted increased risk of developing antibodies against Factor VIII is decreased.

[0133] In another embodiment, the method further comprises adjusting the dosage and/or
30 frequency of Factor VIII administration in a combination therapy based on the predicted risk of

developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0134] In another embodiment, the method further comprises adjusting the dosage and/or frequency of a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0135] In another embodiment, the method further comprises adjusting the dosage and/or frequency of both Factor VIII and a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In this fashion, a combination therapy may be optimized for an individual with a specific predicted risk of developing antibodies against FVIII. Optimization of the dosage and/or frequency of Factor VIII and non-FVIII hemostatic agents in combination therapy may be achieved by any combination of increasing the frequency of FVIII administration, decreasing the frequency of FVIII administration, increasing the dosage of FVIII, decreasing the dosage of FVIII, increasing the frequency of non-FVIII hemostatic agent administration, decreasing the frequency of non-FVIII hemostatic agent administration, increasing the dosage of a non-FVIII hemostatic agent, and decreasing the dosage of a non-FVIII hemostatic agent.

[0136] In a specific embodiment, the method comprises increasing the frequency and/or dosage of FVIII and decreasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0137] In another specific embodiment, the method comprises decreasing the frequency and/or dosage of FVIII and increasing the frequency and/or dosage of a non-FVIII hemostatic agent

administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0138] In a preferred embodiment, the method comprises the detection of at least one SNP selected from those listed in Table 4. In a specific embodiment, the method comprises the
 5 detection of at least on SNP selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888. In one embodiment, at least one detected SNP is rs12368829. In another embodiment, at least one detected SNP is rs4147385. In another embodiment, at least one detected SNP is rs11744216. In another
 10 embodiment, at least one detected SNP is rs1863993. In another embodiment, at least one detected SNP is rs17535213. In another embodiment, at least one detected SNP is rs10072056. In another embodiment, at least one detected SNP is rs10054825. In another embodiment, at least one detected SNP is rs12546235. In another embodiment, at least one detected SNP is rs4242389. In another embodiment, at least one detected SNP is rs2071336. In another
 15 embodiment, at least one detected SNP is rs414634. In another embodiment, at least one detected SNP is rs17725712. In another embodiment, at least one detected SNP is rs11773821. In another embodiment, at least one detected SNP is rs8005905. In another embodiment, at least one detected SNP is rs9482888.

b) After Initial Factor VIII Therapy

20 [0139] In one embodiment, the present invention relates specifically to an individual or group of individuals diagnosed with severe Hemophilia A that have previously received Factor VIII therapy (*i.e.*, received treatment comprising administration of Factor VIII).

[0140] In one embodiment, a method is provided for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with severe Hemophilia A, who
 25 has previously received treatment comprising administration of FVIII, comprising detecting the presence of at least one single nucleotide polymorphism (SNP) selected from the group consisting of a SNP listed in Table 2 and a SNP listed in Table 4, in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII.

[0141] In one embodiment of the method, the individual has been diagnosed with mild
 30 Hemophilia. In another embodiment, the individual has been diagnosed with moderate

Hemophilia. In yet another embodiment, the individual has been diagnosed with severe Hemophilia.

[0142] In one embodiment of the method, the step of detecting the presence of at least one SNP comprises amplifying a nucleic acid present in the biological sample. In another
5 embodiment, the step of detecting the presence of at least one SNP comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, solid phase sequencing, a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.

10 [0143] In one embodiment, the method further comprises assigning and/or administering a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, treatment comprising administration of Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is assigned to an
15 individual with a predicted increased risk of developing antibodies against Factor VIII.

[0144] In yet another specific embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is assigned to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is assigned to an individual with a predicted decreased risk of developing antibodies against Factor
20 VIII. In another specific embodiment, a combination therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0145] In one embodiment, treatment comprising administration of Factor VIII is provided to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another specific embodiment, treatment comprising Factor VIII bypass therapy is provided to an
25 individual with a predicted increased risk of developing antibodies against Factor VIII.

[0146] In yet another embodiment, combination therapy comprising administration of Factor VIII and a FVIII bypass agent is provided to an individual based on the predicted risk of developing antibodies against Factor VIII. In one specific embodiment, a combination therapy is provided to an individual with a predicted decreased risk of developing antibodies against Factor
30 VIII. In another specific embodiment, a combination therapy is provided to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0147] In one embodiment, the method further comprises adjusting a dosage of a treatment comprising administration of Factor VIII to the individual based on the predicted risk of developing antibodies against Factor VIII. In a specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII is increased. In another specific embodiment, a dosage of Factor VIII to be administered to an individual with a predicted increased risk of developing antibodies against Factor VIII is decreased.

[0148] In another embodiment, the method further comprises adjusting the dosage and/or frequency of Factor VIII administration in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of Factor VIII administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0149] In another embodiment, the method further comprises adjusting the dosage and/or frequency of a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In one embodiment, the method comprises increasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted increased risk of developing antibodies against Factor VIII. In another embodiment, the method comprises decreasing the dosage or frequency of a non-FVIII hemostatic agent administered in a combination therapy to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0150] In another embodiment, the method further comprises adjusting the dosage and/or frequency of both Factor VIII and a non-FVIII hemostatic agent administered in a combination therapy based on the predicted risk of developing antibodies against FVIII. In this fashion, a combination therapy may be optimized for an individual with a specific predicted risk of developing antibodies against FVIII. Optimization of the dosage and/or frequency of Factor VIII and non-FVIII hemostatic agents in combination therapy may be achieved by any combination of increasing the frequency of FVIII administration, decreasing the frequency of FVIII administration, increasing the dosage of FVIII, decreasing the dosage of FVIII, increasing the

frequency of non-FVIII hemostatic agent administration, decreasing the frequency of non-FVIII hemostatic agent administration, increasing the dosage of a non-FVIII hemostatic agent, and decreasing the dosage of a non-FVIII hemostatic agent.

[0151] In a specific embodiment, the method comprises increasing the frequency and/or dosage of FVIII and decreasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII.

[0152] In another specific embodiment, the method comprises decreasing the frequency and/or dosage of FVIII and increasing the frequency and/or dosage of a non-FVIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.

[0153] In a preferred embodiment, the method comprises the detection of at least one SNP selected from those listed in Table 4. In a specific embodiment, the method comprises the detection of at least one SNP selected from the group consisting of rs12368829, rs4147385, rs11744216, rs1863993, rs17535213, rs10072056, rs10054825, rs12546235, rs4242389, rs2071336, rs414634, rs17725712, rs11773821, rs8005905, and rs9482888. In one embodiment, at least one detected SNP is rs12368829. In another embodiment, at least one detected SNP is rs4147385. In another embodiment, at least one detected SNP is rs11744216. In another embodiment, at least one detected SNP is rs1863993. In another embodiment, at least one detected SNP is rs17535213. In another embodiment, at least one detected SNP is rs10072056. In another embodiment, at least one detected SNP is rs10054825. In another embodiment, at least one detected SNP is rs12546235. In another embodiment, at least one detected SNP is rs4242389. In another embodiment, at least one detected SNP is rs2071336. In another embodiment, at least one detected SNP is rs414634. In another embodiment, at least one detected SNP is rs17725712. In another embodiment, at least one detected SNP is rs11773821. In another embodiment, at least one detected SNP is rs8005905. In another embodiment, at least one detected SNP is rs9482888.

B. Predictive Markers

[0154] Among other aspects, the present invention provides novel markers consisting of SNPs for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual

diagnosed with Hemophilia A. Any individual SNP provided in Tables 1 to 4 may be used in conjunction with any other individual SNP provided in Tables 1 to 4 in the methods provided herein for the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia A.

5 [0155] As such, the present invention contemplates methods for detecting the identity of the nucleotide corresponding to the genomic position of any single SNP listed in Tables 1 to 4 in a biological sample from an individual diagnosed with Hemophilia A. In another embodiment, the method comprises detecting the identity of the nucleotide corresponding to the genomic position of at least 2 SNPs listed in Tables 1 to 4 in a sample from an individual diagnosed with
10 Hemophilia A. In yet other embodiments, methods are provided for detecting the identity of the nucleotide corresponding to the genomic position of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92,
15 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189,
20 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, more, or all of the SNPs listed in Tables 1 to 4.

[0156] In a related embodiment, the present invention contemplates methods for detecting the presence of any SNP listed in Tables 1 to 4 in a biological sample from an individual diagnosed
25 with Hemophilia A. In another embodiment, the method comprises detecting the presence of at least 2 SNPs listed in Tables 1 to 4 in a sample from an individual diagnosed with Hemophilia A. In yet other embodiments, methods are provided for detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59,
30 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127,

- 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, more, or all of the SNPs listed in Tables 1 to 4. Generally, detecting the presence of at least one SNP in a biological sample from an individual diagnosed with Hemophilia A may comprise detecting the identity of the nucleotide corresponding to the genomic position of multiple SNPs listed in Tables 1 to 4.
- 10 [0157] In certain embodiments, these SNPs may be used in conjunction with other markers known in the art as useful to help predict the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia A. Non-limiting examples of other markers include, various epitopes and allelic variations of the Factor VIII gene and gene product (*see*, Millar DS *et al.*, *Hum Genet.* 1990 Dec;86(2):219-27; Kazazian HH Jr *et al.*, *Nature* 1988 Mar 15 10;332(6160):164-6; and Ostertag EM *et al.*, *Annu Rev Genet.* 2001;35:501-38).

- [0158] Genomic information regarding the SNPs listed in Tables 1 to 4 can be obtained from the ENTREZ SNP database accessible via the website for the National Center for Biotechnology Information (NCBI). For example, as can be found on the server mentioned above, SNP
- 20 rs12368829 corresponds to an A/G single nucleotide polymorphism (SNP) at position 94,473,201 of human chromosome 12 according to build 37.1 of the Celera whole genome sequence. The sequence flanking the SNP comprises the following sequence, with the SNP position underlined in brackets:
- TTGCCACTACTTGTCTCCAAAGAAACA/GTAAGAATGCTTTATCATAACAAGT
- 25 (SEQ ID NO:1). Based on the sequence information provided by the NCBI server, one of skill in the art will readily be able to determine the identity of the nucleotide at a position corresponding to any one of the SNPs listed in Tables 1 to 4 in a biological sample from an individual diagnosed with Hemophilia A.

- [0159]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1003854. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1003854 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1003854 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0160]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10054825. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10054825 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10054825 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0161] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10072056. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10072056 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10072056 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0162] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1007212. In one embodiment, a method is provided for predicting the risk
of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs1007212 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1007212 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0163] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10074391. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10074391 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10074391 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0164]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1007822. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1007822 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1007822 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0165]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10104302. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10104302 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10104302 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0166] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10165797. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10165797 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10165797 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0167] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10261447. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10261447 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10261447 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0168] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10406354. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10406354 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10406354 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0169]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1041067. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1041067 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1041067 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0170]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1044141. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1044141 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1044141 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0171] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1046780. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1046780 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1046780 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0172] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10497208. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10497208 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10497208 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0173] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1050382. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1050382 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1050382 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0174]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10514071. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10514071 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10514071 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0175]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1058240. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1058240 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1058240 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0176] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1062069. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1062069 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1062069 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0177] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1075846. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1075846 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1075846 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0178] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10772120. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10772120 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10772120 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0179] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10789841. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10789841 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10789841 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0180] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10797666. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10797666 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10797666 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0181] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10807350. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10807350 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10807350 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0182] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10836342. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10836342 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10836342 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0183] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10854166. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10854166 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10854166 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0184] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10972149. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10972149 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10972149 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0185] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs10977434. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs10977434 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs10977434 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0186] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11015985. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11015985 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11015985 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0187] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11032349. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11032349 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11032349 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0188] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1105238. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1105238 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1105238 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0189] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11168267. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11168267 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11168267 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0190] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11214108. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11214108 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11214108 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0191] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11237451. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11237451 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11237451 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0192] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11265416. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11265416 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11265416 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0193] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1131510. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1131510 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1131510 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0194]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11574113. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11574113 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11574113 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0195]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11740298. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11740298 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11740298 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0196] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11744216. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11744216 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11744216 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0197] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11773821. In one embodiment, a method is provided for predicting the risk
of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs11773821 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11773821 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0198] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11780679. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11780679 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11780679 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0199]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11833550. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11833550 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11833550 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0200]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11852361. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11852361 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11852361 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0201] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs11952962. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs11952962 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs11952962 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0202] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12001295. In one embodiment, a method is provided for predicting the risk
of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs12001295 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12001295 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0203] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12034383. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12034383 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12034383 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0204]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12039194. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12039194 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12039194 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0205]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12051769. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12051769 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12051769 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0206] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1206486. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1206486 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1206486 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0207] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12185980. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12185980 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12185980 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0208] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12310405. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12310405 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12310405 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0209]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12325842. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 5 comprising the steps of detecting the presence SNP rs12325842 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12325842 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the
- 10 method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method
- 15 further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- 20 **[0210]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12368829. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 25 comprising the steps of detecting the presence SNP rs12368829 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12368829 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the
- 30 individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0211] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12451415. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12451415 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12451415 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0212] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12506181. In one embodiment, a method is provided for predicting the risk
of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs12506181 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12506181 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0213] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12546235. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12546235 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12546235 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0214]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12546235. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12546235 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12546235 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0215]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12625871. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12625871 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12625871 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0216] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1264456. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1264456 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1264456 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0217] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12667537. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12667537 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12667537 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0218] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1267843. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1267843 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1267843 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0219]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12692566. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12692566 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12692566 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0220]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12810163. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12810163 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12810163 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0221] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12814009. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12814009 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12814009 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0222] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12831813. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12831813 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12831813 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0223] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12881815. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12881815 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12881815 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0224]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12959952. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12959952 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12959952 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0225]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs12969613. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs12969613 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs12969613 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0226] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs13042473. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs13042473 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs13042473 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0227] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs13096099. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs13096099 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs13096099 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0228] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs13172280. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs13172280 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs13172280 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0229]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs13173943. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs13173943 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs13173943 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0230]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs13206518. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs13206518 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs13206518 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0231] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1378796. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1378796 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1378796 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0232] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1411479. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1411479 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1411479 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0233] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1436522. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1436522 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1436522 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0234]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1457238. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 5 comprising the steps of detecting the presence SNP rs1457238 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1457238 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the
- 10 method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method
- 15 further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- 20 **[0235]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1465073. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1465073 in a biological sample from the
- 25 individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1465073 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the
- 30 individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0236] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1519602. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1519602 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1519602 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0237] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1523474. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1523474 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1523474 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0238] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1552323. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1552323 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1552323 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0239]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1567748. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1567748 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1567748 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0240]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1573706. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1573706 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1573706 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0241] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs161021. In one embodiment, a method is provided for predicting the risk of
10 developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs161021 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs161021 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising
15 administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be
20 administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs
25 listed in Tables 1, 2, 3, and 4.

[0242] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs161042. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising
30 the steps of detecting the presence SNP rs161042 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs161042 is predictive of a decreased risk of developing antibodies against

Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0243] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1638006. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1638006 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1638006 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0244] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs169142. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs169142 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs169142 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0245] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17110948. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17110948 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17110948 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0246] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17113227. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17113227 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17113227 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0247] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17141840. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17141840 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17141840 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0248] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17201075. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17201075 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17201075 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0249]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17228097. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17228097 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17228097 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0250]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1724120. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1724120 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1724120 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0251] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17283264. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17283264 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17283264 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0252] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17317153. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17317153 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17317153 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0253] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17419586. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17419586 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17419586 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0254]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17535213. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17535213 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17535213 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0255]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17652304. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17652304 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17652304 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0256] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17671456. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17671456 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17671456 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0257] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17725712. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17725712 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17725712 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0258] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17748322. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17748322 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17748322 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0259]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17763453. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17763453 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17763453 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0260]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17811425. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17811425 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17811425 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0261] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17815972. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17815972 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17815972 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0262] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1781795. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1781795 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1781795 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0263] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17834679. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17834679 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17834679 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0264]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs17875513. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs17875513 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs17875513 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0265]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1797646. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1797646 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1797646 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0266] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1797647. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1797647 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1797647 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0267] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1838065. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1838065 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1838065 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0268] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1863993. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1863993 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1863993 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0269]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1865462. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1865462 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1865462 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0270]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1877563. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1877563 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1877563 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0271] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1882019. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1882019 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1882019 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0272] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1884564. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs1884564 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1884564 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0273] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1885831. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1885831 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1885831 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0274]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1892803. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 5 comprising the steps of detecting the presence SNP rs1892803 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1892803 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the
- 10 method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method
- 15 further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- 20 **[0275]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1918309. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 25 comprising the steps of detecting the presence SNP rs1918309 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1918309 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the
- 30 individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0276] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1983165. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1983165 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1983165 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0277] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs1984399. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs1984399 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs1984399 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0278] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2010452. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2010452 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2010452 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0279]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2020902. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2020902 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2020902 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0280]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2069933. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2069933 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2069933 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0281] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2070123. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2070123 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2070123 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0282] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2070783. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2070783 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2070783 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0283] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2071081. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2071081 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2071081 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0284]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2071336. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2071336 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2071336 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0285]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2076620. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2076620 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2076620 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0286] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2076846. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2076846 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2076846 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0287] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs208250. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising
30 the steps of detecting the presence SNP rs208250 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs208250 is predictive of an increased risk of developing antibodies against

Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0288] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs210431. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs210431 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs210431 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0289]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2157605. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2157605 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2157605 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0290]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2163057. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2163057 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2163057 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0291] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2179694. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2179694 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2179694 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0292] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2227562. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs2227562 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2227562 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0293] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2227827. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2227827 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2227827 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0294]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2231375. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2231375 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2231375 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0295]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2238337. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2238337 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2238337 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0296] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2242660. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2242660 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2242660 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0297] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2255364. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2255364 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2255364 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0298] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2267908. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2267908 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2267908 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0299]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2268890. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2268890 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2268890 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0300]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2275603. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2275603 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2275603 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0301] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2278324. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2278324 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2278324 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0302] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2279590. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2279590 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2279590 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0303] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2283539. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2283539 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2283539 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0304]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2286414. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2286414 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2286414 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0305]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2287768. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2287768 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2287768 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0306] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2288522. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2288522 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2288522 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0307] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2295616. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2295616 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2295616 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0308] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2296449. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2296449 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2296449 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0309]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2298877. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2298877 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2298877 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0310]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2302267. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2302267 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2302267 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0311] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2302759. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2302759 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2302759 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0312] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2302821. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2302821 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2302821 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0313] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2305340. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2305340 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2305340 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0314] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2335478. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2335478 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2335478 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0315] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs241430. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs241430 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs241430 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be

administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0316] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs244076. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs244076 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs244076 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0317] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs244090. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs244090 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs244090 is predictive of an increased risk of developing antibodies against

Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0318] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs244091. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs244091 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs244091 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0319] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs244656. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs244656 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs244656 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0320] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs246390. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs246390 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs246390 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be

administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0321] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs246392. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs246392 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs246392 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0322] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs246394. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs246394 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs246394 is predictive of a decreased risk of developing antibodies against

Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0323] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs246395. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs246395 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs246395 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0324]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2569190. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 5 comprising the steps of detecting the presence SNP rs2569190 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2569190 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the
- 10 method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method
- 15 further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- 20 **[0325]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2575674. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2575674 in a biological sample from the
- 25 individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2575674 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the
- 30 individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0326] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2584019. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2584019 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2584019 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0327] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2595204. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2595204 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2595204 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0328] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2596606. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2596606 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2596606 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0329]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2838733. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2838733 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2838733 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0330]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2844463. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2844463 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2844463 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0331] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2853884. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2853884 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2853884 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0332] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2869460. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2869460 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2869460 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0333] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2869461. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2869461 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2869461 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0334]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs2879097. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs2879097 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs2879097 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0335]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3024486. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3024486 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3024486 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0336] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3024498. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3024498 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3024498 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another
20 embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0337] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs304839. In one embodiment, a method is provided for predicting the risk of
30 developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs304839 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs304839 is predictive of an increased risk of developing antibodies against

Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0338] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs310247. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs310247 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs310247 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0339]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs31519. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs31519 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs31519 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0340]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3181096. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3181096 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3181096 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0341] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3211821. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3211821 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3211821 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0342] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3211834. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3211834 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3211834 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0343] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3733236. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3733236 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3733236 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0344]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3733678. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3733678 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3733678 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0345]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3736101. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3736101 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3736101 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0346] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3736395. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3736395 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3736395 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0347] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3788151. In one embodiment, a method is provided for predicting the risk
30 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3788151 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3788151 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0348] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3795326. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3795326 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3795326 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0349]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3797390. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3797390 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3797390 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0350]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3815003. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3815003 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3815003 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0351] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3816724. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3816724 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3816724 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0352] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3819496. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs3819496 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3819496 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
5 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
10 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0353] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
15 consisting of SNP rs3826392. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3826392 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one
20 embodiment, the presence of SNP rs3826392 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
25 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
30 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0354]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3828016. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3828016 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3828016 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0355]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs3845422. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs3845422 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs3845422 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0356] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs390406. In one embodiment, a method is provided for predicting the risk of
10 developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs390406 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs390406 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising
15 administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be
20 administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs
25 listed in Tables 1, 2, 3, and 4.

[0357] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4027402. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs4027402 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4027402 is predictive of a decreased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0358] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4077341. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4077341 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4077341 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0359]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4094864. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4094864 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4094864 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0360]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4104. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4104 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4104 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be

administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0361] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs414634. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs414634 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs414634 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0362] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4147385. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4147385 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4147385 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0363] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs424051. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs424051 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs424051 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0364]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4242389. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4242389 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4242389 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- [0365]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4245886. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4245886 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4245886 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0366] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4251520. In one embodiment, a method is provided for predicting the risk
10 of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4251520 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4251520 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a
15 therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0367] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4253655. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 comprising the steps of detecting the presence SNP rs4253655 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4253655 is predictive of an increased risk of developing

antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0368] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs440238. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs440238 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs440238 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

- [0369]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4462251. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
- 5 comprising the steps of detecting the presence SNP rs4462251 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4462251 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the
- 10 method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method
- 15 further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.
- 20 **[0370]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4472605. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4472605 in a biological sample from the
- 25 individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4472605 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the
- 30 individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
5 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0371] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
10 consisting of SNP rs4485556. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4485556 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4485556 is predictive of an increased risk of developing
15 antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another
20 embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0372] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs4498385. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4498385 in a biological sample from the

individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4498385 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0373] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4572808. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4572808 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4572808 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0374] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4639174. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4639174 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4639174 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0375] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4646077. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4646077 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4646077 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a

therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group
5 consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0376] In one embodiment, the present invention provides a marker useful for predicting the
10 risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4698806. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4698806 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one
15 embodiment, the presence of SNP rs4698806 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
20 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
25 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0377] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs4724231. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4724231 in a biological sample from the

individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4724231 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

15 **[0378]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4752894. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4752894 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4752894 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0379] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4752896. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4752896 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4752896 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0380] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4752904. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4752904 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4752904 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a

therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group
5 consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0381] In one embodiment, the present invention provides a marker useful for predicting the
10 risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4756331. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4756331 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one
15 embodiment, the presence of SNP rs4756331 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
20 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
25 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0382] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs4798598. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4798598 in a biological sample from the

individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4798598 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

15 [0383] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4820059. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4820059 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4820059 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0384] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4902264. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4902264 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4902264 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0385] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4953292. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4953292 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4953292 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a

therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group
5 consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0386] In one embodiment, the present invention provides a marker useful for predicting the
10 risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4955104. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4955104 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one
15 embodiment, the presence of SNP rs4955104 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
20 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
25 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0387] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs4955272. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4955272 in a biological sample from the

individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4955272 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

15 [0388] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs4966019. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs4966019 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs4966019 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0389] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs496888. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs496888 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs496888 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0390] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs499205. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs499205 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs499205 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in
5 Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0391] In one embodiment, the present invention provides a marker useful for predicting the
10 risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs509749. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs509749 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the
15 presence of SNP rs509749 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising
20 administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the
25 presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0392] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs5743220. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs5743220 in a biological sample from the

individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs5743220 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

15 **[0393]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs5743740. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs5743740 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs5743740 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0394] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs5746154. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs5746154 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs5746154 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0395] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs599563. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs599563 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs599563 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising

administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in
5 Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0396] In one embodiment, the present invention provides a marker useful for predicting the
10 risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs5996577. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs5996577 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one
15 embodiment, the presence of SNP rs5996577 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
20 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
25 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0397] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs6016685. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs6016685 in a biological sample from the

individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs6016685 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

15 **[0398]** In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs6021183. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs6021183 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs6021183 is predictive of an increased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0399] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs6058391. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs6058391 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs6058391 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0400] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs6060855. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs6060855 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one embodiment, the presence of SNP rs6060855 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a

therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group
5 consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0401] In one embodiment, the present invention provides a marker useful for predicting the
10 risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A consisting of SNP rs6065460. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs6065460 in a biological sample from the individual; and predicting the risk of the individual of developing antibodies to FVIII. In one
15 embodiment, the presence of SNP rs6065460 is predictive of a decreased risk of developing antibodies against Factor VIII. In one embodiment, the method further comprises assigning a therapy comprising administration of Factor VIII to the individual. In another embodiment, the method further comprises assigning a therapy comprising Factor VIII bypass therapy to the individual. In another embodiment, the method further comprises increasing a dosage of a
20 therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises decreasing a dosage of a therapy comprising administration of FVIII to be administered to the individual. In another embodiment, the method further comprises detecting the presence of at least a second SNP selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4. In another embodiment, the method further
25 comprises detecting the presence of at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or more SNPs selected from the group consisting of the SNPs listed in Tables 1, 2, 3, and 4.

[0402] In one embodiment, the present invention provides a marker useful for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A
30 consisting of SNP rs6065467. In one embodiment, a method is provided for predicting the risk of developing antibodies against FVIII in an individual diagnosed with Hemophilia A comprising the steps of detecting the presence SNP rs6065467 in a biological sample from the

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CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 191

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JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 191

NOTE: For additional volumes, please contact the Canadian Patent Office

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CLAIMS:

1. A method for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, the method comprising the steps of
 - (a) detecting the presence of one or more single nucleotide polymorphisms (SNPs) in a biological sample from the individual, wherein the one or more SNPs comprises T>C variant at SNP rs13206518, wherein presence of the T>C variant at SNP rs13206518 indicates a decreased risk of the individual developing antibodies to FVIII; and
 - (b) predicting the risk of the individual of developing antibodies to FVIII based on the one or more SNPs.
2. The method of claim 1, wherein an odds ratio of less than 1 from the one or more SNPs collectively is predictive of a decreased risk of developing antibodies against FVIII and an odds ratio of more than 1.0 from the one or more SNPs collectively is predictive of an increased risk of developing antibodies against FVIII.
3. The method of claim 1 or 2, wherein the individual either: (i) has not received therapy comprising administration of FVIII; or (ii) has received therapy comprising administration of FVIII.
4. The method according to any one of claims 1 to 4, wherein the individual has been diagnosed with mild Hemophilia.
5. The method according to any one of claims 1 to 4, wherein the individual has been diagnosed with moderate Hemophilia.
6. The method according to any one of claims 1 to 4, wherein the individual has been diagnosed with severe Hemophilia.
7. The method according to any one of claims 1 to 6, wherein the step of detecting the presence of the one or more SNPs comprises amplifying a nucleic acid present in the biological sample.
8. The method according to any one of claims 1 to 7, wherein the step of detecting the presence of the one or more SNPs comprises amplifying a nucleic acid and further
 - (i) comprises a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, and solid phase sequencing, or

(ii) comprises a method selected from the group consisting of a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.

9. The method according to any one of claims 1 to 8, wherein step (a) comprises
 5 detecting the presence of at least the following SNPs in a biological sample from the individual: T>C variant at SNP rs13206518, and at least one SNP selected from C>G variant at rs11744216, A>C variant at rs3211834, C>T variant at rs1863993, C>T variant at rs4147385, and A>C variant at rs1567748; wherein
 presence of the T>C variant at SNP rs13206518 indicates a decreased risk of the
 10 individual developing antibodies to FVIII;
 presence of the C>G variant at rs11744216 indicates a decreased risk of the individual developing antibodies to FVIII;
 presence of the A>C variant at rs3211834 indicates a decreased risk of the individual developing antibodies to FVIII;
 15 presence of the C>T variant at rs1863993 indicates an increased risk of the individual developing antibodies to FVIII;
 presence of the C>T variant at rs4147385 indicates an increased risk of the individual developing antibodies to FVIII; and
 presence of the A>C variant at rs1567748 indicates a decreased risk of the individual
 20 developing antibodies to FVIII.

10. The method according to any one of claims 1 to 9, wherein the method further comprises assigning a treatment to the individual based on the predicted risk of developing antibodies against Factor VIII.

11. The method of claim 10, wherein the treatment comprises administration
 25 (i) of Factor VIII,
 (ii) of non-Factor VIII hemostatic agent, or
 (iii) of Factor VIII and a non-factor VIII hemostatic agent.

12. The method of claim 10 or 11, wherein treatment comprising administration of Factor VIII is assigned to an individual with a predicted decreased risk of developing antibodies against Factor VIII.
13. The method of claim 10 or 11, wherein treatment comprising Factor VIII
5 bypass therapy is assigned to an individual with a predicted increased risk of developing antibodies against Factor VIII.
14. The method of claim 10 or 11, wherein assigning treatment comprises adjusting a dosage and/or frequency of Factor VIII administration based on the predicted risk of developing antibodies against Factor VIII.
- 10 15. The method of claim 14, wherein adjusting a dosage of Factor VIII comprises
(i) increasing the dosage and/or frequency of Factor VIII administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII, or
(ii) decreasing the dosage and/or frequency of Factor VIII administered to an individual with a predicted increased risk of developing antibodies against Factor VIII.
- 15 16. The method of claim 10 or 11, wherein assigning treatment comprises adjusting a dosage and/or frequency of a non-Factor VIII hemostatic agent administration based on the predicted risk of developing antibodies against Factor VIII.
17. The method of claim 16, wherein adjusting a dosage of a non-Factor VIII hemostatic agent comprises
(i) decreasing the dosage and/or frequency of a non-Factor VIII hemostatic agent
20 administered to an individual with a predicted decreased risk of developing antibodies against Factor VIII, or
(ii) increasing the dosage and/or frequency of a non-Factor VIII hemostatic agent administered to an individual with a predicted increased risk of developing antibodies
25 against Factor VIII.
18. One or more oligonucleotides from 10 to 60 nucleotides in length for use in the method according to any one of claims 1 to 17, wherein the one or more oligonucleotides are capable of detecting T>C variant at SNP rs13206518.

19. The one or more oligonucleotides according to claim 18, further comprising oligonucleotides capable of detecting at least one of the following SNPs: rs13206518, rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748.
20. A diagnostic kit for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, moderate Hemophilia or severe Hemophilia, the kit comprising the one or more oligonucleotides according to claim 18 or 19, and a reagent for carrying out a technique selected from the group consisting of mass spectroscopy, RT-PCR, microarray hybridization, pyrosequencing, thermal cycle sequencing, capillary array sequencing, and solid phase sequencing or for carrying out a method selected from the group consisting of a hybridization-based method, an enzymatic-based method, a PCR-based method, a sequencing method, a ssDNA conformational method, and a DNA melting temperature assay.
21. The diagnostic kit according to claim 20, further comprising oligonucleotides capable of detecting at least one of the following SNPs: rs13206518, rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748.
22. Use of the one or more oligonucleotides according to claim 18 or 19, for predicting the risk of developing antibodies against Factor VIII (FVIII) in an individual diagnosed with Hemophilia, moderate Hemophilia or severe Hemophilia.
23. The use according to claim 22, wherein the one or more oligonucleotides further comprise oligonucleotides capable of detecting at least one of the following SNPs: rs13206518, rs11744216, rs13206518, rs3211834, rs1863993, rs4147385, and rs1567748.