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(54) Title: DRUG DELIVERY DEVICE HAVING TWO DRUG DELIVERY ARRANGEMENTS

(57) Abstract: A drug delivery device (1) comprising a housing unit (2) and at least two drug delivery arrangements (3), each having a drive energy source (8) for providing energy for a drug delivery operation, a medicament container (5) for receiving a drug, and a needle (6), being associated with the respective medicament container, wherein the dual provision of the drug delivery arrangements increases both the dispensing volume and the dispensing speed.

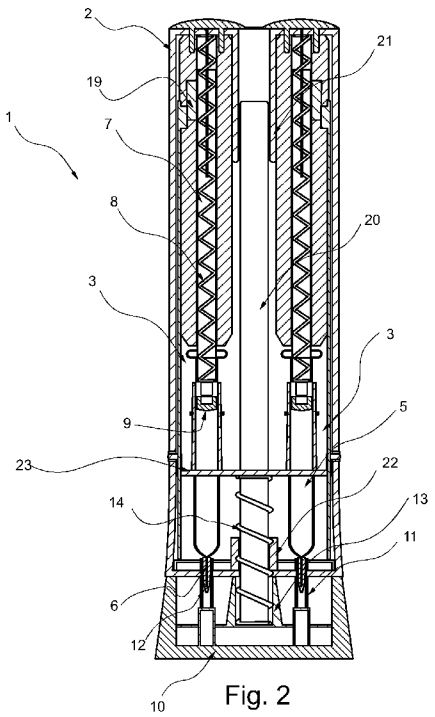

Fig. 2

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[Continued on next page]

SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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Title

Drug delivery device having two drug delivery arrangements

Background

When administering medication through or into a patient's skin, it is desirable that the medication is administered quickly and in sufficient quantity without causing undue pain to the patient. It is especially difficult to meet these requirements when the administration of the medicament has to be carried out by a medically untrained assistant or by the patient himself. The use of drug delivery devices can simplify the administration of medications. However, drug delivery devices are often either cumbersome to operate or have a complex design that results in increased manufacturing costs.

Summary

It is an object of the present disclosure to facilitate improvements associated with drug delivery devices, particularly with respect to manufacturing costs, ease of use, and the ability to deliver drugs within a short period of time.

This object is achieved by subject-matter disclosed herein, for example by the subject-matter defined in the appended independent claim. Advantageous refinements and developments are subject to dependent claims and/or set forth in the description below.

One aspect of the present disclosure relates to a drug delivery device. The drug delivery device may be provided to dispense drug or medicament. The drug delivery device comprises a housing unit. The housing unit may form the outer surface of the drug delivery device and may delimit the drug delivery device from the periphery. The periphery of the drug delivery device may be anything that is external to the housing unit and not physically connected to the housing unit. The housing unit may be held directly by the user's hands when using the drug delivery device. The drug delivery device comprises at least two drug delivery arrangements. The drug delivery device may comprises three, four, five or six drug delivery arrangements. The drug delivery arrangements have a drive energy source, e.g. a drive spring or another type of energy source such as a gas reservoir, for providing energy for a drug delivery operation. The drug delivery device is configured to perform a drug delivery operation, e.g. using energies obtainable from the drive energy sources. Furthermore, each of the drug delivery arrangements

has a medicament container for receiving a drug and a needle, being associated with the respective medicament container. The needles are expediently configured to pierce a skin of a user. Through the needles, the drug may be administered to the user, e.g. into the user's tissue. The energies of the drive energy sources may be used to drive drive members, e.g. plunger rods, of the drug delivery device in order to dispense drug from the medicament containers. For the drug delivery operation, the drive members may be displaced in a distal direction relative to the housing unit by the energies provided by the drive energy sources. The at least two drug delivery arrangements are positioned in the housing unit, such that the medicament containers are fluidically separated with respect to each other, preferably before, during and after a drug delivery operation. In this context, fluidically separated expediently means that there can be no mixing of the contents of the two medicament containers, e.g. at least as long as the two drug delivery arrangements, each having one of the containers, are contained by the housing unit. The contents of the containers may also be administered separately into the body. Each of the two drug delivery arrangements may be configured such that their respective components such as, for example, the drive energy source, the medicament container and/or the needle, are directly enclosed by a respective additional arrangement housing of their own or are directly enclosed by the housing unit.

Due to the dual provision of the components required to deliver the drug, the drug delivery process may be faster and more reliable, wherein a larger quantity of drugs may be administered, e.g. using a similar or identical architecture for all of the delivery arrangements of the device. Furthermore, the patient's perception of pain may be reduced by using two smaller needles instead of one larger needle. Moreover, the fluidically separated medicament containers may help to dispense two different drugs simultaneously with only one device.

In one embodiment the drug delivery device is configured such that the energy of the respective drive energy source of the two drug delivery arrangements can be released simultaneously i.e. at the same time. Likewise, the distal movement of the plunger rods may thus also take place simultaneously. Therefore, the drugs of both medicament containers may be dispensed at the same time. This helps to achieve the administration of larger doses with short injection times. Apart from that, errors can be prevented, such as the user forgetting to administer a required second medicament. Alternatively, the drug delivery device may be configured such that the energy of the respective drive energy source of the two drug delivery arrangements may be released at different times. In this case the dispensing of the drugs from the medicament containers may be sequential and/or overlap in time.

In one embodiment the drug delivery device is configured such that the respective distance between the respective distal tip of the needle (e.g. that end of the needle which pierces the skin) and the distal end of the housing unit of both drug delivery arrangements is the same before the drug delivery operation.

In one embodiment the drug delivery device is configured such that the respective distance between the respective distal tip of the needle and the distal end of the housing unit of both drug delivery arrangements is the same during the drug delivery operation.

In one embodiment the drug delivery device is configured such that the needle tips of the needles pierce the patient's skin simultaneously to each other prior to the drug delivery operation. Alternatively the drug delivery device may be configured such that the needle tips of the needles pierce the patient's skin delayed at different times prior to the delivery process.

In one embodiment the drug delivery device is configured such that the distances between the distal tips of the needles and the distal end of the housing unit are different to each other prior to the drug delivery operation. Accordingly, the tips of the needles may protrude from the housing unit to different extents or by different distances in the distal direction, e.g. before the energies of the drive energy sources of the two drug delivery arrangements have been released. This can help to insert the needle tips into the patient's skin sequentially, e.g. before the drug delivery operation is commenced, rather than simultaneously. Thus, the pain perceived by the patient when piercing the skin may be reduced.

In one embodiment the drug delivery device is configured such that the distances between the distal tips of the needles and the distal end of the housing unit are different to each other during the drug delivery operation. Accordingly, the tips of the needles may protrude from the housing unit to different extents or by different distances in the distal direction, e.g. after the energies of the drive energy sources of the two drug delivery arrangements have been released. The needles may be inserted into the patient's skin with different depths during the drug delivery operation. Therefore, the tissue volume of the skin that is available to absorb the drug may be increased. In addition, two different drugs may be injected at the same time to reach different tissue areas.

In one embodiment the respective medicament container and/or the needle can be axially secured within the drug delivery device, e.g. within housing unit, or can be movable relative to the housing unit, e.g. for piercing the skin. In the first case, the user may have to perform the

movement for piercing the skin with the needles. In the second case, piercing of the needles may be driven by a needle insertion mechanism of the drug delivery device.

In one embodiment the drug delivery device is a single use device. The drug delivery device may be configured to deliver a preset amount of drug. The drug delivery device may be disposed of after its use.

In one embodiment, the drug delivery device is configured such that the drive energy sources and the medicament containers are arranged parallel to each other and/or next to each other in the housing unit. In addition or alternatively, the drug delivery device may be configured such that such that the drive energy sources, the medicament containers and the needles are arranged parallel next to each other in the housing unit. The parallel arrangement may significantly reduce the length of the drug delivery device. This helps in particular to make the drug delivery device more compact and thus more user-friendly. Alternatively, the drug delivery device may be configured such that the drive energy sources, the medicament containers and the needles are arranged offset and/or next to each other in the housing unit. The adjacent arrangement, especially of the needles, allows the drug to be delivered simultaneously or substantially simultaneously to different skin areas. The area of the skin that comes into contact with the drug is thus increased. The patient's body thus absorbs the drug more effectively. Furthermore the increased contact area makes the patient feel better during the injection.

In one embodiment, the respective needle may be in or may be brought into fluid communication with an interior of the respective medicament container. The respective needle may be integrated into the respective medicament container. The medicament, e.g. a liquid medicament, is expediently arranged in the interior of the container. The respective medicament container may be a syringe, e.g. a syringe with a preinstalled needle, such as a staked needle. Alternatively, the respective medicament container may be a cartridge, which may have to be brought into fluid communication with a separate needle unit, e.g. by piercing a cartridge septum with the needle of the needle unit.

In one embodiment, the drug delivery device is an autoinjector. In an autoinjector the energy for the drug delivery operation may be prestored in the drive energy sources. That is to say, the user does not have to provide the energy for the drug delivery operation, e.g. when preparing the device for use. Rather, this energy may be preloaded into the system by the manufacturer. For example, a drive spring may be pre-stressed or pre-biased to provide the energy for the drug delivery operation.

In one embodiment, the respective needle, e.g. when received in the housing unit, is axially fixed relative to the housing unit. That is to say, axial movement of the needle relative to the housing unit may be prevented, preferably in the distal direction and/or in the proximal direction. The respective needle may be fixed with respect to the housing unit of the drug delivery device. We note however, that the presently disclosed concepts do also apply to a drug delivery device comprising or provided to retain a respective movable needle which is configured to move relative to the housing unit, e.g. driven by a spring, for piercing the skin and/or for the drug delivery operation.

In one embodiment, each of the drug delivery arrangements is configured to perform a drug delivery operation by releasing the respective energy of the drive energy source in order to dispense the drug when the respective drug delivery arrangement is positioned in the housing unit and when the respective drug delivery arrangement is separated from the housing unit. Each drug delivery arrangement may comprise the respective arrangement housing, configured to enclose the respective drive energy source, medicament container and needle. The respective arrangement housing may be configured to be held by the user when performing a drug delivery operation of the respective drug delivery arrangement when the drug delivery arrangement is separated from the housing unit. One of the two or both drug delivery arrangements may be an autoinjector. Furthermore, one of the two or both drug delivery arrangements may be single shot devices, i.e. they are provided to dispense only one dose.

In one embodiment, one of the two or both drug delivery arrangements comprise a needle shroud. The respective needle shroud may be provided to cover the respective needle. The needle shroud may be provided to cover the respective needle before the needle pierces the skin and/or after the needle has been removed from the skin, e.g. after completion of the drug delivery operation. Before the drug delivery operation is commenced, the respective needle shroud may protrude distally from the respective arrangement housing (and the housing unit), e.g. to cover the tip of the needle (such as by axially extending beyond the tip of the needle in the distal direction). For the drug delivery operation, the respective needle shroud may be displaced proximally relative to the arrangement housing (and the housing unit). After completion of the drug delivery operation, the needle shroud may be moved distally relative to the arrangement housing, e.g. to cover the tip of the needle.

Each of the two drug delivery arrangements may comprise a respective shroud spring. The shroud spring may be operatively coupleable to or coupled to the needle shroud in order to move the needle shroud, e.g. into the distal direction relative to the respective arrangement housing when the arrangement or the device is removed from the skin. The force of the shroud

spring may have to be overcome in order to move the needle shroud in the proximal direction away from an initial position. In a final position, e.g. after the drug delivery operation has been completed, the arrangement has been removed from the skin and/or the shroud spring has displaced the needle shroud distally, the needle shroud may be locked against proximal movement with respect to the arrangement housing, such as by a locking mechanism.

In one embodiment, the respective needle shroud of the drug delivery arrangement is an activation member. An activation member is a member which may have to be moved relative to the arrangement housing in order to enable triggering of the drug delivery operation or to trigger the drug delivery operation. Enable triggering of the drug delivery operation may comprise that in addition to movement of the activation member another member such as a trigger member has to be actuated, e.g. a trigger button has to be pressed. Alternatively, the needle shroud itself may be the trigger member. Thus, when the needle shroud reaches a trigger position, the drug delivery operation may be initiated, e.g. resulting in the plunger rod being moved in the distal direction relative to the arrangement housing.

In one embodiment the housing unit comprises at least two receiving chambers, wherein each of the receiving chambers is configured to receive and axially secure one of the two drug delivery arrangements, e.g. in a removable manner, preferably repeatedly removable manner. This allows the drug delivery device to be reloaded with one or more drug delivery arrangements after the drug delivery operation has been conducted. Alternatively, each, or one of the receiving chambers may be configured to receive and axially secure one of the two drug delivery arrangements in a permanent and/or non-removable manner. The drug delivery device is thus suitable to use already long proven drug delivery arrangements by accommodating them in the receiving chambers. This makes it possible to completely avoid the redesign of proven functional components, e.g. with respect to the fixation in the housing unit.

In one embodiment the two drug delivery arrangements are two different arrangements, and the drug delivery arrangements may differ in external dimensions, shape and/or in the way of operation. Alternatively, the two drug delivery arrangements may be two identical arrangements, and the drug delivery arrangements may be identical in external dimensions, shape and/or in the way of operation.

In one embodiment the two receiving chambers are configured such that the drug delivery device is able to perform the drug delivery operation regardless of in which of the two receiving chambers one of the two drug delivery arrangement is received and secured in.

In one embodiment the length of at least one of the receiving chambers is at most 95%, 90%, 85% or 80% of the length of the housing unit.

In one embodiment the length of at least one of the receiving chambers is at least 55%, 60%, 65%, 70% or 75% of the length of the housing unit.

In one embodiment the length of at least one of the receiving chambers is at most 95%, 90%, 85% or 80% and at least 55%, 60%, 65%, 70% or 75% of the length of the housing unit.

In one embodiment the length of each of the receiving chambers is the same. Alternatively, the length of each of the receiving chambers may be different.

In one embodiment the diameter of each of the receiving chambers is the same. Alternatively, the diameter of each of the receiving chambers may be different.

In one embodiment the diameter of at least one of the receiving chambers may vary, e.g. along its axial extension. A distal diameter may be greater than a proximal diameter.

In one embodiment each of the receiving chambers has an opening in the distal end region of the respective receiving chamber. The respective opening may be configured to allow the respective drug delivery arrangement to be inserted into the receiving chamber through the opening. The openings may be arranged side by side and/or parallel within the housing unit. The openings may face in the same direction.

In one embodiment each of the receiving chambers is closed in the proximal end region of the respective receiving chamber. The respective closed proximal end region may provide a stop surface for the respective drug delivery arrangement to prevent the drug delivery arrangement against further movement in the proximal direction after the drug delivery arrangement has been received by the receiving chamber.

In one embodiment, the stop surfaces may be arranged parallel to each other within the housing unit. Additionally, the stop surfaces may be arranged side by side within the housing unit. The parallel adjacent stop surfaces thus delimit the receiving chambers at the same section along the longitudinal axis of the housing unit, so that the two receiving chambers have the same insertion depth for receiving the respective drug delivery arrangement. If two drug delivery arrangements of the same length are secured in the receiving chambers of the housing unit, the insertion of the needles and / or the drug delivery operation may take place simultaneously.

Alternatively, the stop surfaces may also be arranged parallel and laterally offset. The parallel lateral offset of the stop surfaces may thus limit the receiving chambers at different sections along the longitudinal axis of the housing unit, so that the two receiving chambers have a different insertion depth for receiving the respective drug delivery arrangement. If two drug delivery arrangements of the same length are inserted and secured in the housing unit, the insertion of the needles and / or the drug delivery operation may take place at different times.

In one embodiment at least one of the two receiving chambers has a distal end region in which the inner diameter decreases continuously in the proximal direction to facilitate insertion of the drug delivery arrangement through the opening into the receiving chamber. The inner diameter of the distal end portion may be conical.

In one embodiment, the distal end region may be at least 5%, 10%, 15%, 20% or 25% of the length of the receiving chamber.

In one embodiment, the distal end region may be at most 30%, 35% or 45% of the length of the receiving chamber.

In one embodiment, the distal end region may be at least 5%, 10%, 15%, 20% or 25% and at most 30%, 35% or 45% of the length of the receiving chamber.

In one embodiment each of the drug delivery arrangements has a respective cap connected to the respective arrangement housing. At least one of the respective receiving chambers may be configured such that, when the drug delivery arrangement is secured in the receiving chamber, the respective cap protrudes at least sufficiently from the opening of the receiving chamber to allow a user to grasp the cap in order to separate the cap from the arrangement housing.

In one embodiment the radial distance between the central longitudinal axes of the two receiving chambers is greater than the diameter of the drug delivery arrangement with the cap at its largest position.

In one embodiment, the length of the receiving chamber is at most so long that the proximal end region of the cap attached on the drug delivery arrangement, is completely outside the receiving chamber when the drug delivery arrangement is fully received up to the stop surface. This helps to provide a known and trouble-free removal of the cap.

In one embodiment at least one of the receiving chambers comprises at least one fixation member for fixating the respective drug delivery arrangement in the receiving chamber. The fixation member may secure the drug delivery arrangement against axial and rotational movement relative to the housing unit.

In one embodiment each of the receiving chambers comprises at least one fixation member. The fixation members of the two receiving chambers may be arranged side by side in parallel to each other. Alternatively, the fixation members of the two receiving chambers may be arranged offset to each other.

In one embodiment one of or each of the drug delivery arrangements has at least one recess providing a window. The window is preferably arranged in the arrangement housing. The window may be configured to allow at least a portion of the medicament container to be seen through the window. The medicament container may be transparent. The window may be adapted to provide information about the state of the drug delivery arrangement, such as whether or not a drug delivery operation has been conducted. The fixation member may comprise a protrusion configured to engage the recess of the window to lock the drug delivery arrangement in the receiving chamber against distal, proximal and/or rotational movement relative to the housing unit. The drug delivery arrangement or its arrangement housing may be fixed in the receiving chamber by a form-fit connection.

In one embodiment at least one of the receiving chambers comprises two fixation members which are spaced axially offset from each other. The two fixation members may be axially offset from each other along the inner circumferential surface of the receiving chamber by more than 1/4, 1/3, 1/2, 2/3 or 3/4 of the length of the receiving chamber.

In one embodiment the respective fixation member is an O-shaped ring or O-ring. The O-shaped ring may be elastically deformable. The drug delivery arrangement or its arrangement housing may be fixed in the receiving chamber by a friction-fit connection.

In one embodiment the drug delivery device comprises a needle shroud, configured to cover and enclose both of the two needles of the respective drug delivery arrangements. The needle shroud may be an integral component, i.e. a one-piece or unitary component. The needle shroud may be provided to cover both of the needles before the needles pierces the skin and/or after the needles have been removed from the skin, e.g. after completion of the drug delivery operations of both drug delivery arrangements. Before the drug delivery operation is commenced, the needle shroud may protrude distally from the housing unit, e.g. to cover the

tips of the needles, such as by axially extending beyond the tips of needles in the distal direction. For the drug delivery operation, the needle shroud may be displaced proximally relative to the housing unit. After completion of the drug delivery operation, the needle shroud may be moved distally relative to the housing unit, e.g. to cover the tips of needles. The needle shroud may be axially movable relative to the needles.

In one embodiment the drug delivery device may comprise a shroud spring. The shroud spring may be operatively coupleable to or coupled to the needle shroud in order to move the needle shroud, e.g. into the distal direction relative to the housing unit. The force of the shroud spring may have to be overcome in order to move the needle shroud in the proximal direction away from an initial position. The shroud spring may be configured to move the needle shroud in a distal direction, e.g. in order to cover the tips of two needles after the drug delivery operation is complete and the drug delivery device has been removed from the skin. The needle shroud may be locked against proximal movement with respect to the housing unit, such as by a needle shroud locking mechanism in a distal end or final position. The needle shroud spring may be located between the two medicament containers and/or needles inside of the housing unit.

In one embodiment, the needle shroud of the drug delivery device is an activation member. The needle shroud may have to be moved relative to the housing unit in order to enable triggering of the drug delivery operation or to trigger the drug delivery operation of both drug delivery arrangements. Enable triggering of the drug delivery operations may comprise that in addition to movement of the needle shroud another member such as a trigger member has to be actuated, e.g. a trigger button has to be pressed. Alternatively, the needle shroud itself may be the trigger member. Thus, when the needle shroud reaches a trigger position, the drug delivery operations may be initiated, e.g. the energy from the both drive energy sources may be released and the plunger rods being moved in the distal direction relative to the housing unit. The drug delivery operations may include simultaneous release of energy from both drive energy sources. Alternatively, the drug delivery operation may include release of the energy from both drive energy sources at different times. The release of the respective energy from the drive energy sources may overlap in time, e.g. such that the delivery from the different containers may start sequentially but occur simultaneously for a certain time.

In one embodiment the drug delivery device is configured such that the release of the respective energy from the drive energy sources is triggered by a movement of the needle shroud relative to the needles.

In one embodiment the needle shroud is configured to be axially movable relative to the housing unit between the initial position and the final position. Additionally, the needle shroud may be configured to cover the respective needle by extending axially beyond the tip of the needle in the distal direction in both the initial position and the final position. Furthermore, in addition, the needle shroud may be configured to extend further in the distal direction in the final position than in the initial position.

In one embodiment the drug delivery device comprises a container carrier configured to bear the two medicament containers inside the housing unit. The container carrier may be an integral component, i.e. a one-piece component.

In one embodiment the drug delivery device comprises a clicker configured to provide an audible signal to the user after the dispensing of the medications stored in the two medicament containers is complete.

In one embodiment the drug delivery device comprises a cap configured to cover the distal end portions, e.g. the needle ends, of the two medicament containers. The cap may be an integral component, i.e. a one-piece component. The cap may be removable or detachable from the housing unit.

In one embodiment the cap comprises at least two needle shield removers, configured to grip and remove a respective needle shield of the respective needles.

Providing a drug delivery device that requires only one housing, clicker, cap, container carrier, needle shroud and/or needle shroud spring for simultaneous or substantially simultaneous dispensing of at least two drugs from two separate and adjacent medicament containers helps to significantly reduce the complexity of the device design, by avoiding unnecessary duplicate provision of features. Furthermore, the overall weight of the drug delivery device as well as its manufacturing costs may thus be reduced. Additionally, the adaption of the design allows to reduce unnecessary plastic waste.

We note that features described above and below in conjunction with different embodiments or aspects can be combined with one another, even if such a combination is not explicitly disclosed herein above or below. Further features, advantages and expediencies of the disclosure and, particularly, of the proposed concepts will become apparent from the following description of the exemplary embodiments in conjunction with the drawings.

Brief description of the drawings

Figure 1 illustrates a sectional side view of a first embodiment of a drug delivery device having two drug delivery arrangements.

Figures 2 and 3A illustrate a sectional side view of a second embodiment of a drug delivery device having two drug delivery arrangements prior to a drug delivery operation.

Figure 3B illustrates another sectional side view of the second embodiment prior to a drug delivery operation.

Figure 3C illustrates another sectional side view of the second embodiment during a drug delivery operation.

Figure 3D illustrates another sectional side view of the second embodiment after a drug delivery operation.

Figure 4 illustrates an expanded structural formula, molecular formula, and molecular weight of fitusiran.

Description of exemplary embodiments

The term “distal” is used herein to specify directions, ends or surfaces which are arranged or are to be arranged to face or point towards a dispensing end of the drug delivery device or the drug delivery arrangements or components thereof. On the other hand, “proximal” is used to specify directions, ends or surfaces which are arranged or are to be arranged to face away from or point away from the dispensing end and/or from the distal end of the drug delivery device or the drug delivery arrangements or components thereof. The distal end may be the end closest to the dispensing end and/or furthest away from the proximal end and the proximal end may be the end furthest away from the dispensing end. A proximal surface may face away from the distal end and/or towards the proximal end. A distal surface may face towards the distal end and/or away from the proximal end. The dispensing end may be the tip of the needles, for example.

The first embodiment shown in Figure 1 and the second embodiment shown in Figures 2-3D differ in that in the second embodiment, only one housing, clicker, cap, container carrier, needle shroud and needle shroud spring is provided to perform both dispensing operations. The drug

delivery arrangements shown in Figure 1 and Figures 2-3D are very similar to the device disclosed in WO 2015/004052 A1, the entire disclosure content of which is incorporated herein by reference for all purposes, especially with respect to the design of the drive mechanism or "plunger release mechanism" as it is termed therein.

The Figures 1-3D illustrate a drug delivery device 1 according to the invention. The drug delivery device 1 is provided to dispense a drug or medicament. The drug delivery device 1 comprises a housing unit 2 and two drug delivery arrangements 3. In the first embodiment depicted in Figure 1, the drug delivery arrangements 3 each additionally have their own arrangement housing 4, and both drug delivery arrangements 3 can perform the drug delivery operation regardless of whether or not they are fixed in the housing unit 2. In the second embodiment depicted in Figures 2-3D, the drug delivery arrangements 3 do not have an additional housing of their own. Accordingly, the housing unit 2 of both drug delivery arrangements 3 is the housing unit 2 that directly surrounds the drug delivery arrangements 3. In this case, both drug delivery arrangements 3 can only perform the drug delivery operation when they are installed in the housing unit 2.

For each drug delivery arrangement 3, the housing unit 2 is provided to retain and/or retains (either indirectly with the use of the arrangement housings 4 in the first embodiment of Figure 1 or directly in the second embodiment of Figures 2-3D) a respective medicament container 5 in its interior. Medicament, e.g. liquid medicament, is arranged in the medicament container 5. Likewise for each drug delivery arrangement 3, the housing unit 2 is provided to retain and/or retains a respective needle 6. In other words, the needles 6 may be arranged or arrangeable in the respective arrangement housings 4 (Figure 1) or directly in the housing unit 2 (Figure 2-3D). The needle 6 can be an integral part of the medicament container 5, e.g. (permanently or releasably) connected to a medicament container body, or separate from the medicament container 5. In the first case, the medicament container 5 may be a syringe. In the second case, the medicament container 5 may be a cartridge. In case a cartridge is used as medicament container 5, initially, the medicament container 5 and the needle 6 can be fluidly disconnected and fluid communication between the medicament container interior and the needle 6 is only established during operation of the drug delivery arrangement 3. The two drug delivery arrangements 3 are positioned in the housing unit 2, such that the medicament containers 5 are fluidically separated with respect to each other before, during and after a drug delivery operation. The respective needles 6 in Figure 1 and Figures 2-3D are axially fixed relative to the housing unit 2. Axial movement of the needles 6 relative to the housing unit 2 is prevented in the distal and proximal direction. We note however, that both depicted embodiments may

also comprise a respective movable needle which is configured to move relative to the housing unit.

According to the first embodiment in Figure 1, a drive mechanism provided to drive a drug delivery operation is expediently provided in each of the arrangement housings 4. With regard to the second embodiment in Figures 2-3D, two drive mechanisms are provided in the housing unit 2. The respective drive mechanism comprises a plunger rod 7. Each drug delivery arrangement 3 further comprises a drive energy source 8, e.g. a drive spring, such as a compression spring. The drive energy source 8 is arranged to drive the plunger rod 7 in a distal direction relative to the medicament container 5 during the drug delivery operation. During this movement, a stopper 9, which is movably retained in the medicament container 5 and may seal the medicament container 5 proximally, can be displaced towards an outlet of the medicament container 5 to dispense the drug or medicament retained within the medicament container 5 through the outlet. The outlet may be formed or defined by the respective needle 6. Other potential drive energy sources different from a spring comprise an electrical power cell or battery for driving the plunger rod 7 by a motor or a reservoir suitable to provide gas pressure, where the gas pressure can be used to drive the drug delivery operation. In the depicted embodiment of Figure 1 each of the drug delivery arrangements 3 is an autoinjector. The drug delivery arrangements 3 according to Figure 1 are expediently single shot devices. In the depicted embodiment of Figures 2-3D the drug delivery device 1 is an auto injector. The medicament containers 5, the needles 6 and the drive energy sources 8 according to both embodiments are arranged parallel next to each other in the housing unit 2.

It should be noted that in both the first embodiment and the second embodiment, features of the drug delivery arrangements 3, such as the respective needles 8, the medicament containers 5, and/or the drive energy sources 8, can be arranged adjacent to each other in an offset manner in the axial direction of the housing unit 2. As described below, this can be used in particular to influence the timing of insertion of the two needles 8, as well as the depth of insertion and the timing of the respective drug delivery operation.

As depicted in Figure 1, two caps 10 are arranged at the distal end of each of the drug delivery arrangements 3. The respective cap 10 is detachably connected to the remainder of the drug delivery arrangement 3, e.g. to the arrangement housing 4 and/or another component or member of the drug delivery arrangement 3. The respective cap 10, e.g. with a distally oriented surface, covers a distal end of the remainder of the respective drug delivery arrangement 3 and/or a needle passage opening through which the respective needle 6, e.g. the distal needle tip, may pass to pierce the skin from the interior of drug delivery arrangement 3 during or for the

drug delivery operation. The respective cap 10 can comprise a needle shield remover 11, which engages a needle shield 12, e.g. a rigid needle shield or a soft needle shield, which covers the needle 6 such that the needle shield remover 11 is removed from the needle 6 together with the cap 10, e.g. when the cap 10 is detached or disconnected from the respective drug delivery arrangement 3. The arrangement housing 4 expediently covers the majority of the length of the drug delivery arrangement 3, e.g. 60% or more or 70% or more or 80% or more of the entire length of the drug delivery arrangement 3 (with the cap 10 attached and/or with the cap 10 detached).

The respective needle shield 12 may be axially and/or rotationally locked to the respective cap 10 such that it is removed together with the cap 10, e.g. by prongs or barbs provided in the cap 10. When the cap 10 is rotated, the needle shield 12 may rotate as well relative to the arrangement housing 4. The respective medicament container 5 may rotate as well relative to the respective arrangement housing 4 or be rotationally locked relative to the arrangement housing 4 e.g. by according rotational stops. If the medicament container 5 rotates together with the needle shield 12, there is no relative rotational movement between the needle shield 12 and the needle 6, such that the risk of damages to the needle 6 may be reduced. Further, the cap 10 may be configured such that the connection between the cap 10 and the corresponding drug delivery arrangement 3 may be removed solely by axial movement of the cap 10 relative to the housing unit 2.

As depicted in Figure 1, each drug delivery arrangement 3 further comprises a needle shroud 13. The respective needle shroud 13 protrudes distally from the respective arrangement housing 4 and/or is covered by the cap 10 when the cap 10 is attached to the arrangement housing 4. The needle shroud 13 is movable relative to the arrangement housing 4 from an initial or first shroud position A to a second shroud position B. The respective needle shroud 13 may be provided to extend beyond the tip of the respective needle 6 which may protrude from the arrangement housing 4 before the drug delivery operation is commenced. The needle shroud 13 is movable in the proximal direction relative to the arrangement housing 4. During this movement, e.g. before the needle shroud 13 reaches the second shroud position B, the needle 6 may pierce the skin of the user. The needle shroud 13 can serve as a trigger member of the drug delivery arrangement 3. The needle shroud 13 as trigger member, when displaced proximally from the first shroud position A to the shroud position B, may automatically initialize the drug delivery operation, preferably when it is in the second shroud position B. After completion of the drug delivery operation, the respective needle shroud 13 may be moved distally relative to the respective arrangement housing 4 to a third shroud position C to cover the tip of the respective needle 6.

The drug delivery operation of the respective drug delivery arrangement 3 is initialized by removing a respective mechanical lock which prevents movement of the plunger rod 7 in the distal direction or by moving plunger rod 7 to disengage a mechanical lock via the moving needle shroud 13. Alternatively, the needle shroud 13 when moved from the first shroud position A to the second shroud position B and expediently when in the second shroud position B may only enable triggering of the respective drug delivery operation. In this case, a separate trigger member, e.g. a trigger button on the proximal end of the arrangement housing 4, may be provided to initiate the drug delivery operation. Operating the trigger button to initiate the drug delivery operation may only be possible when the needle shroud 13 is in the second shroud position B. In yet another alternative, the needle shroud 13 may only be provided to prevent needle stick injuries before and/or after use of the drug delivery device. In this case, the needle shroud 13 may be completely decoupled from the drive mechanism and/or not be involved in triggering or enabling triggering of the drug delivery operation at all.

With respect to both embodiments (Figure 1 and Figures 2-3D), it should be noted that if the energy of the drive energy sources is released at different times, both embodiments can be designed in such a way that the user can choose the timing of the first and second drug delivery operation. This may be enabled, for example, by each of the drug delivery arrangements 3 having a trigger button that can be operated by the user. For example, for emergency medications that could have significant side effects, a "full dose" and a "half dose" could be dispensed, selected based on whether medical help is available soon.

Each of the two drug delivery arrangements 3 comprises a shroud spring 14. The respective shroud spring 14 is operatively coupled to the needle shroud 13 in order to move the needle shroud 13 into the distal direction relative to the respective arrangement housing 4 when the arrangement 3 or the device 1 is removed from the skin. The force of the shroud spring 14 has to be overcome in order to move the needle shroud 13 in the proximal direction away from the first shroud position A. In a final or third shroud position C after the drug delivery operation has been completed, the respective drug delivery arrangement 3 has been removed from the skin and the shroud spring 14 has displaced the needle shroud 13 distally, the respective needle shroud 13 is locked against proximal movement with respect to the arrangement housing 4.

The depicted embodiment of Figure 1 shows two receiving chambers 15, wherein each of the receiving chambers 15 is configured to receive and axially secure one of the two drug delivery arrangements 3 in a repeatedly removable manner. The radial distance between the central longitudinal axes of the two receiving chambers 15 is greater than the diameter of the one of the

drug delivery arrangements 3 with the cap 10 at its largest position. The two drug delivery arrangements 3 are identical. Therefore the two drug delivery arrangements 3 are identical in external dimensions, shape and in the way of operation. In addition, both receiving chambers 15 share the same inner dimensions. As a result, the drug delivery device 1 is able to perform the drug delivery operation regardless of which of the two receiving chambers 15 the respective drug delivery arrangement 3 is secured in. Each receiving chamber 15 has an opening 16 in the distal end region of the respective receiving chamber 15. The respective opening 16 allows the respective drug delivery arrangement 3 to be inserted into the receiving chamber 16, wherein the openings are arranged side by side and parallel within the housing unit 2. Both receiving chambers 15 are closed in the proximal end region. The respective closed proximal end region has a stop surface 17. The stop surface 17 prevents the drug delivery arrangement 3 against further movement in the proximal direction after the drug delivery arrangement 3 is received by the receiving chamber 15. The two stop surfaces 17 are arranged side by side and parallel to each other. Since both the parallel arranged receiving chambers 15 and the drug delivery arrangements 3 are identical, needle insertion and drug delivery operation may occur simultaneously. As shown, each of the two receiving chambers 15 has a distal end region with a cone in which the inner diameter decreases continuously in the proximal direction.

Each of the receiving chambers 15 comprises two fixation members 18. The fixation members 18 fixate the respective drug delivery arrangement 3 against axial and rotational movement relative to the housing unit 2 by a friction-fit connection. The fixation members 18 of the two receiving chambers 15 are arranged parallel next to each other. Furthermore the respective fixation members 18 are axially offset from each other along the inner circumferential surface of the respective receiving chamber 15. The respective fixation member 18 is an elastically deformable O-shaped ring. The respective O-shaped ring can be continuously abutting the inner circumferential surface at one position of the receiving chamber 15. The diameter of the O-shaped ring can be equal to the inner diameter of the receiving chamber 15. The respective receiving chamber 15 may additionally have an annular recess in its circumferential surface, the said recess being complementary in shape to the O-shaped ring so that the O-shaped ring can be supported in the recess. The respective recess can prevent axial displacement of the O-shaped ring within the receiving chamber 15 when the drug delivery arrangement 3 is inserted. In an example not shown, the fixation of the respective drug delivery arrangement 3 in the housing unit 2 can also take place by positive locking, i.e. by a form-fit connection. This may be realized by forming the respective fixation member as a protrusion on the inner circumferential surface of the respective receiving chamber 5. This protrusion can engage in a corresponding recess on the surface of the respective drug delivery arrangement 3 when the arrangement is

inserted. This recess can be, for example, a window in the arrangement housing 4 of the drug delivery arrangement 3.

Concerning the first embodiment of the invention shown in Figure 1, it should be noted that the first embodiment, in addition to the simultaneous release of the energy of the drive energy sources 8, can also be implemented in such a way that the release of the energy of the drive energy sources 8 can be offset in time. Regardless of when the release of the energy of both drive energy sources 8 occurs, the two needles 6 of the respective drug delivery arrangements 3 may pierce the patient's skin to the same or different lengths during the drug delivery operation. Similarly, the insertion of the two needle tips may be simultaneous or delayed in time. This can be accomplished, on the one hand, by the features of the two drug delivery arrangements 3 having different dimensions or being subject to different modes of functioning, or by the two receiving chambers 15 having different lengths. Furthermore, it is possible to position the respective fixation members 16 of the two receiving chambers 15 axially offset from each other so that, for example, two identical drug delivery arrangements 3 are fixed in the receiving chamber 15 at different distances in the proximal direction.

As shown in Figures 2-3D, the drug delivery device 1 according to the second embodiment comprises one cap 10, which is arranged at the distal end of the housing unit 10. The cap 10 is detachably connected to the housing unit 2. The cap 10 covers the distal end of the remainder of the drug delivery arrangements 3 and/or needle passage openings through which the respective needles 6, e.g. the distal needle tip, may pass to pierce the skin from the interior of drug delivery arrangements 3 during or for the drug delivery operation. The cap 10 comprises two needle shield removers 11. Each of the needle shield removers 11 engages a respective needle shield 12, e.g. a rigid needle shield or a soft needle shield, which covers the needle 6 such that the needle shields 11 are removed from the needles 6 together with the cap 10, e.g. when the cap 10 is detached or disconnected from the housing unit 2. The two needle shields 12 are axially locked to the cap 10 such that they are removed together with the cap 10, e.g. by prongs or barbs provided in the cap 10.

The drug delivery device 1 according to the second embodiment as shown in Figures 2-3D comprises one needle shroud 13 configured to cover and enclose both of the two needles 6 of the respective drug delivery arrangements 3. The needle shroud 13 protrudes distally from the housing unit 2 and is covered by the cap 10 when the cap 10 is attached to the housing unit 10. The needle shroud 13 is axially movable relative to the housing unit from a first shroud position A (as shown in Figure 2, 3A and 3B) to a second shroud position B (as shown in Figure 3C). The needle shroud 13 is provided to extend beyond the tip of the needles 6 which protrude from

the housing unit 2 before the drug delivery operation is commenced. The needle shroud 13 is movable in the proximal direction relative to the housing unit 2. During this movement, e.g. before the needle shroud 13 reaches the second shroud position B, the needles 6 pierce the skin of the user.

The needles 6 are arranged parallel to each other and are axially fixed relative to the housing unit 2. When the distal end of the needle shroud 13 rests on the patient's skin and the needle shroud 13 is moved from the first shroud position A to the second shroud position B, the two needle tips pierce or puncture the patient's skin simultaneously. The needle shroud 13 serves as a trigger member for the two drug delivery arrangements 3. The needle shroud 13 as trigger member, when displaced proximally from the first shroud position A to the shroud position B, automatically initialize the drug delivery operation, preferably when it is in the second shroud position B (as shown in Figure 3C). The drug delivery operation of the drug delivery arrangements 3 is initialized by removing a respective mechanical lock 19, which prevents movement of the plunger rod 7 in the distal direction or by moving the plunger rod 7 to disengage a mechanical lock 19, positioned at a proximal portion of the respective plunger rod 7, via the moving needle shroud 13. The respective mechanical lock 19 can be released by an elongated portion of the needle shroud 13 extending from the distal front region of the needle shroud 13 in the proximal direction. The mechanical lock 19 for the respective plunger rod 7 shown in Figures 2-3D is a variant in which a locking function is used on only one side of the plunger rod 7. However, it should be noted that it is possible to use a locking function on more than one, such as two, sides of the respective plunger rod 7. Furthermore, it is possible that the respective plunger rod 7 is alternatively or additionally unlocked by the needle shroud 13 at a distal front portion of the plunger rod 7. In this case the mechanical lock 19 may be positioned at a distal portion of the respective plunger rod 7. By unlocking the respective plunger rod 7 through the needle shroud 13 at a front distal portion of the plunger rod 7, the elongated portion of the needle shroud 13 extending from the distal front region of the needle shroud 13 in the proximal direction may be made much shorter.

As mentioned above, especially with respect to the design of a respective plunger release mechanism, reference is made to the entire content of WO 2015/004052 A1, which is incorporated herein. Alternatively, the needle shroud 13 when moved from the first shroud position A to the second shroud position B and expediently when in the second shroud position B may only enable triggering of the drug delivery operation. In this case, a separate trigger member (not shown), e.g. a trigger button on the proximal end of the housing unit 2, ca be provided to initiate the drug delivery operation. Operating the trigger button to initiate the drug delivery operation may only be possible when the needle shroud 13 is in the second shroud

position B. In yet another alternative, the needle shroud 13 may only be provided to prevent needle stick injuries before and/or after use of the drug delivery device. In this case, the needle shroud 13 may be completely decoupled from the drive mechanism and/or not be involved in triggering or enabling triggering of the drug delivery operation at all.

Figure 3C illustrates the needle shroud 13 in the second shroud position B relative to the housing unit 4. This is the position when the drug delivery operation has been initiated, can be initiated, and/or when the needles 6 pierce the skin (not shown), for example. The drug delivery device 1 is maintained in contact with the skin until the drug delivery operation has been completed, which may be indicated by an audible, tactile, and/or visual indication provided by the drug delivery device 1. After the drug delivery operation has been completed, the drug delivery device 1 is removed from the skin (see Figure 3D). The needle shroud 13 is biased relative to the housing unit 2 towards the first shroud position A by a shroud spring 14. Thus, when the drug delivery device 1 is removed from the skin the needle shroud 13 is moved towards the first shroud position A or beyond its first shroud position A, into a final, locked or third shroud position C relative to the housing unit 2 as shown in Figure 3D. In the third shroud position C the needle shroud 13 is expediently axially locked relative to the housing unit 2 against movement in the proximal direction, e.g. by a locking engagement between a locking feature, such as a flexible clip, of the needle shroud 13 and the housing unit 2. As it is axially locked, the needle shroud 13 can no longer be displaced proximally relative to the housing unit 2 into the second and/or into the first shroud position. This protects the user from needle stick injuries after use. In addition, it may no longer be possible to reattach the cap 10 when the needle shroud 13 is in the third shroud position C. To secure the needle shroud 13 against axial movement relative to the housing unit 2, the needle shroud 13 may have several clips. For example, the needle shroud 13 may have four, five, six, seven, eight or more clips. The clips may each be spaced the same distance from each other along the circumference of the needle shroud 13. Furthermore, it is also conceivable that the clips are arranged opposite one another.

As can be seen in Figures 3B and 3D, the needle shroud 13 is configured to be axially movable relative to the housing unit 2 between the first shroud position A, i.e. the initial position, and the third shroud position C, i.e. the final position. In both the initial position A and the final position C, the needle shroud 13 covers the respective needle 6 by extending axially beyond the tip of the needle 6 in the distal direction. In positions A and C, the needle shroud 13 protrudes over the needle tips of both needles at the same time. The comparison between Figures 3B and 3D shows in particular that the needle shroud 13 extends further in the distal direction in the final position C (see Figure 3D) than in the initial position A (see Figure 3B).

In the embodiment shown in Figure 1, the drug delivery device also comprises a needle shroud 13. In this case, the needle shroud 13 comprises two separately movable needle shrouds. The needle shrouds are axially movable relative to the housing unit 2 between the initial position A and the final position C. The needle shrouds cover the respective associated needle 6 by extending axially beyond the associated needle tip in the distal direction both in the initial position A and in the final position C. Both needle shrouds extend further in the distal direction in the final position C than in the initial position A.

As shown in Figures 2-3D, the shroud spring 14 is mounted on a guide rod 20, which is enclosed by the shroud spring. The guide rod 20 can be an integral part of the needle shroud 13. The guide rod 20 can be axially movable relative to the housing unit 2. The housing unit 2 comprises two proximal guiding members 21. The two proximal guiding members 21 are arranged parallel next to each other. The two proximal guiding members 21 may bear, enclose and guide the proximal portion of the guide rod 20. In addition the two proximal guiding members 21 may bear and separate the proximal portions of the drug delivery arrangements 3, such as proximal portions of the drive energy sources 8 and the plunger rods 7. Moreover, the drug delivery device 1 may comprise two parallel arranged distal guiding members 22, configured to bear, enclose and guide the distal portion of the guide rod 20. The two distal and proximal guiding members 21 and 22 provide a tight guiding of the guide rod 20 that ensures that no tilting occurs, which otherwise may result in the release of only one drive energy source 8. The needle shroud spring 14 and the guide rod 20 are located between the two medicament containers 5 and the two needles 6 in the interior of the housing unit 2. The depicted drug delivery device 1 further comprises a container carrier 23 configured to bear the two medicament containers 5 inside the housing unit 2. In addition, the container carrier 23 may abut the proximal end of the shroud spring 14.

The drug delivery device 1 depicted in Figures 2-3D can be configured to release the energy of both dive energy sources 8 simultaneously. In this context, the phrase “release of the energy of one/both drive energy sources” includes the distal movement of the respective plunger rod 7 and the respective ejection of the drug from the needle tip. The drug delivery device 1 can also be configured to release the energy of both drive energy sources 8 slightly offset in time. Accordingly, the drug delivery operation of one of the drug delivery arrangements 3 can start after the drug delivery operation of the remaining drug delivery arrangement 3 has already started but before the drug delivery operation of the remaining drug delivery arrangement 3 has been completed. Likewise, the drug delivery operation of one of the drug delivery arrangements 3 can start after the drug delivery operation of the remaining drug delivery arrangement 3 has already started and directly after the drug delivery operation of the remaining drug delivery arrangement 3 has been completed. Regardless of whether the energy of both dive energy

sources 8 is released simultaneously offset in time, both needles 6 can have the same depth of injection into the patient's skin. Alternatively, both needles 6 can have a different depth of injection into the patient's skin, wherein this can be achieved, for example, by the needle tips of the two needles 6 protruding from the housing unit 2 to different extents and/or having different lengths. Further, regardless of whether the needles 6 have a different depth of injection, the insertion of the needles 6 can be simultaneous or offset in time. Simultaneous insertion of the needle tips at different injection depths can be achieved, for example, by providing at least one of the needles 6 of the drug delivery arrangements 3 with a movable structure relative to the housing unit 2.

It is further possible that both drug delivery arrangements 3 each comprise a rear subassembly comprising the plunger rod 7 and the drive energy source 8. The rear subassembly can be a skeleton structure that secures the plunger rod 7 and the drive energy source 8 in the housing unit 2. The rear subassembly can also be mounted and secured in the respective proximal guide member 21. Additionally, the rear subassembly may comprise the clicker. The rear subassembly may be designed to be replaced after a drug deliver operation so that the housing unit 2 can be reused.

It should be noted that both embodiments can also contain more than two, such as three, four, five or six drug delivery arrangements 3, which are positioned parallel side by side or axially offset to one another directly or indirectly through a respective arrangement housing 4 in the housing unit 2.

Furthermore, in both embodiments, it is possible for the respective needle shroud 13 (Figure 1) or the single needle shroud 13 (Figure 2-3D) to move slightly in the distal direction immediately after the cap 10 is removed but before the needle shroud 13 is placed on the skin surface and before the plunger rod 7 and the energy of the drive energy sources 8 is released. In this case, the needle shroud 13 slides forward slightly, since the shroud spring 14 is released and the plunger rod 7 rotates to a position where it is ready for use. In particular, this may be the case when the cap 10 is directly engaged with the arrangement housing 4 of the drug delivery arrangement 3 or the housing unit 2.

The terms “drug” or “medicament” are used synonymously herein and describe a pharmaceutical formulation containing one or more active pharmaceutical ingredients or pharmaceutically acceptable salts or solvates thereof, and optionally a pharmaceutically acceptable carrier. An active pharmaceutical ingredient (“API”), in the broadest terms, is a chemical structure that has a biological effect on humans or animals. In pharmacology, a drug

or medicament is used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being. A drug or medicament may be used for a limited duration, or on a regular basis for chronic disorders.

As described below, a drug or medicament can include at least one API, or combinations thereof, in various types of pharmaceutical formulations, for the treatment of one or more diseases. Examples of API may include small molecules having a molecular weight of 500 Da or less; polypeptides, peptides and proteins (e.g., hormones, growth factors, antibodies, antibody fragments, and enzymes); carbohydrates and polysaccharides; and nucleic acids, double or single stranded DNA (including naked and cDNA), RNA, antisense nucleic acids such as antisense DNA and RNA, small interfering RNA (siRNA), ribozymes, genes, and oligonucleotides. Nucleic acids may be incorporated into molecular delivery systems such as vectors, plasmids, or liposomes. Mixtures of one or more drugs are also contemplated.

The drug or medicament may be contained in a primary package or "drug reservoir" adapted for use with a drug delivery device. The drug reservoir 101a may be, e.g., a cartridge, syringe, reservoir, or other solid or flexible vessel (bag) configured to provide a suitable chamber for storage (e.g., short- or long-term storage) of one or more drugs. For example, in some instances, the chamber may be designed to store a drug for at least one day (e.g., 1 to at least 30 days). In some instances, the chamber may be designed to store a drug for about 1 month to about 2 years. Storage may occur at room temperature (e.g., about 20°C), or refrigerated temperatures (e.g., from about - 4°C to about 4°C). In some instances, the drug reservoir may be or may include a dual-chamber cartridge configured to store two or more components of the pharmaceutical formulation to-be-administered (e.g., an API and a diluent, or two different drugs) separately, one in each chamber. In such instances, the two chambers of the dual-chamber cartridge may be configured to allow mixing between the two or more components prior to and/or during dispensing into the human or animal body. For example, the two chambers may be configured such that they are in fluid communication with each other (e.g., by way of a conduit between the two chambers) and allow mixing of the two components when desired by a user prior to dispensing. Alternatively or in addition, the two chambers may be configured to allow mixing as the components are being dispensed into the human or animal body.

The drugs or medicaments contained in the drug delivery devices as described herein can be used for the treatment and/or prophylaxis of many different types of medical disorders. Examples of disorders include, e.g., diabetes mellitus or complications associated with diabetes mellitus such as diabetic retinopathy, thromboembolism disorders such as deep vein or

pulmonary thromboembolism. Further examples of disorders are acute coronary syndrome (ACS), angina, myocardial infarction, cancer, macular degeneration, inflammation, hay fever, atherosclerosis and/or rheumatoid arthritis. Examples of APIs and drugs are those as described in handbooks such as Rote Liste 2014, for example, without limitation, main groups 12 (anti-diabetic drugs) or 86 (oncology drugs), and Merck Index, 15th edition.

Examples of APIs for the treatment and/or prophylaxis of type 1 or type 2 diabetes mellitus or complications associated with type 1 or type 2 diabetes mellitus include an insulin, e.g., human insulin, or a human insulin analogue or derivative, a glucagon-like peptide (GLP-1), GLP-1 analogues or GLP-1 receptor agonists, or an analogue or derivative thereof, a dipeptidyl peptidase-4 (DPP4) inhibitor, or a pharmaceutically acceptable salt or solvate thereof, or any mixture thereof. As used herein, the terms “analogue” and “derivative” refers to a polypeptide which has a molecular structure which formally can be derived from the structure of a naturally occurring peptide, for example that of human insulin, by deleting and/or exchanging at least one amino acid residue occurring in the naturally occurring peptide and/or by adding at least one amino acid residue. The added and/or exchanged amino acid residue can either be codable amino acid residues or other naturally occurring residues or purely synthetic amino acid residues. Insulin analogues are also referred to as "insulin receptor ligands". In particular, the term „derivative” refers to a polypeptide which has a molecular structure which formally can be derived from the structure of a naturally occurring peptide, for example that of human insulin, in which one or more organic substituent (e.g. a fatty acid) is bound to one or more of the amino acids. Optionally, one or more amino acids occurring in the naturally occurring peptide may have been deleted and/or replaced by other amino acids, including non-codeable amino acids, or amino acids, including non-codeable, have been added to the naturally occurring peptide.

Examples of insulin analogues are Gly(A21), Arg(B31), Arg(B32) human insulin (insulin glargine); Lys(B3), Glu(B29) human insulin (insulin glulisine); Lys(B28), Pro(B29) human insulin (insulin lispro); Asp(B28) human insulin (insulin aspart); human insulin, wherein proline in position B28 is replaced by Asp, Lys, Leu, Val or Ala and wherein in position B29 Lys may be replaced by Pro; Ala(B26) human insulin; Des(B28-B30) human insulin; Des(B27) human insulin and Des(B30) human insulin.

Examples of insulin derivatives are, for example, B29-N-myristoyl-des(B30) human insulin, Lys(B29) (N- tetradecanoyl)-des(B30) human insulin (insulin detemir, Levemir®); B29-N-palmitoyl-des(B30) human insulin; B29-N-myristoyl human insulin; B29-N-palmitoyl human insulin; B28-N-myristoyl LysB28ProB29 human insulin; B28-N-palmitoyl-LysB28ProB29 human insulin; B30-N-myristoyl-ThrB29LysB30 human insulin; B30-N-palmitoyl- ThrB29LysB30 human

insulin; B29-N-(N-palmitoyl-gamma-glutamyl)-des(B30) human insulin, B29-N-omega-carboxypentadecanoyl-gamma-L-glutamyl-des(B30) human insulin (insulin degludec, Tresiba®); B29-N-(N-lithocholyl-gamma-glutamyl)-des(B30) human insulin; B29-N-(ω-carboxyheptadecanoyl)-des(B30) human insulin and B29-N-(ω-carboxyheptadecanoyl) human insulin.

Examples of GLP-1, GLP-1 analogues and GLP-1 receptor agonists are, for example, Lixisenatide (Lyxumia®), Exenatide (Exendin-4, Byetta®, Bydureon®, a 39 amino acid peptide which is produced by the salivary glands of the Gila monster), Liraglutide (Victoza®), Semaglutide, Taspoglutide, Albiglutide (Syncria®), Dulaglutide (Trulicity®), rExendin-4, CJC-1134-PC, PB-1023, TTP-054, Langlenatide / HM-11260C (Efpeglenatide), HM-15211, CM-3, GLP-1 Eligen, ORMD-0901, NN-9423, NN-9709, NN-9924, NN-9926, NN-9927, Nodexen, Viador-GLP-1, CVX-096, ZYOG-1, ZYD-1, GSK-2374697, DA-3091, MAR-701, MAR709, ZP-2929, ZP-3022, ZP-DI-70, TT-401 (Pegapamodtide), BHM-034. MOD-6030, CAM-2036, DA-15864, ARI-2651, ARI-2255, Tirzepatide (LY3298176), Bamadutide (SAR425899), Exenatide-XTEN and Glucagon-Xten.

An example of an oligonucleotide is, for example: mipomersen sodium (Kynamro®), a cholesterol-reducing antisense therapeutic for the treatment of familial hypercholesterolemia or RG012 for the treatment of Alport syndrom.

Examples of DPP4 inhibitors are Linagliptin, Vildagliptin, Sitagliptin, Denagliptin, Saxagliptin, Berberine.

Examples of hormones include hypophysis hormones or hypothalamus hormones or regulatory active peptides and their antagonists, such as Gonadotropine (Follitropin, Lutropin, Choriongonadotropin, Menotropin), Somatropine (Somatropin), Desmopressin, Terlipressin, Gonadorelin, Triptorelin, Leuprorelin, Buserelin, Nafarelin, and Goserelin.

Examples of polysaccharides include a glucosaminoglycane, a hyaluronic acid, a heparin, a low molecular weight heparin or an ultra-low molecular weight heparin or a derivative thereof, or a sulphated polysaccharide, e.g. a poly-sulphated form of the above-mentioned polysaccharides, and/or a pharmaceutically acceptable salt thereof. An example of a pharmaceutically acceptable salt of a poly-sulphated low molecular weight heparin is enoxaparin sodium. An example of a hyaluronic acid derivative is Hylan G-F 20 (Synvisc®), a sodium hyaluronate.

The term “antibody”, as used herein, refers to an immunoglobulin molecule or an antigen-binding portion thereof. Examples of antigen-binding portions of immunoglobulin molecules include F(ab) and F(ab')2 fragments, which retain the ability to bind antigen. The antibody can be polyclonal, monoclonal, recombinant, chimeric, de-immunized or humanized, fully human, non-human, (e.g., murine), or single chain antibody. In some embodiments, the antibody has effector function and can fix complement. In some embodiments, the antibody has reduced or no ability to bind an Fc receptor. For example, the antibody can be an isotype or subtype, an antibody fragment or mutant, which does not support binding to an Fc receptor, e.g., it has a mutagenized or deleted Fc receptor binding region. The term antibody also includes an antigen-binding molecule based on tetravalent bispecific tandem immunoglobulins (TBTI) and/or a dual variable region antibody-like binding protein having cross-over binding region orientation (CODV).

The terms “fragment” or “antibody fragment” refer to a polypeptide derived from an antibody polypeptide molecule (e.g., an antibody heavy and/or light chain polypeptide) that does not comprise a full-length antibody polypeptide, but that still comprises at least a portion of a full-length antibody polypeptide that is capable of binding to an antigen. Antibody fragments can comprise a cleaved portion of a full length antibody polypeptide, although the term is not limited to such cleaved fragments. Antibody fragments that are useful in the present invention include, for example, Fab fragments, F(ab')2 fragments, scFv (single-chain Fv) fragments, linear antibodies, monospecific or multispecific antibody fragments such as bispecific, trispecific, tetraspecific and multispecific antibodies (e.g., diabodies, triabodies, tetrabodies), monovalent or multivalent antibody fragments such as bivalent, trivalent, tetravalent and multivalent antibodies, minibodies, chelating recombinant antibodies, tribodies or bibodies, intrabodies, nanobodies, small modular immunopharmaceuticals (SMIP), binding-domain immunoglobulin fusion proteins, camelized antibodies, and VHH containing antibodies. Additional examples of antigen-binding antibody fragments are known in the art.

The terms “Complementarity-determining region” or “CDR” refer to short polypeptide sequences within the variable region of both heavy and light chain polypeptides that are primarily responsible for mediating specific antigen recognition. The term “framework region” refers to amino acid sequences within the variable region of both heavy and light chain polypeptides that are not CDR sequences, and are primarily responsible for maintaining correct positioning of the CDR sequences to permit antigen binding. Although the framework regions themselves typically do not directly participate in antigen binding, as is known in the art, certain residues within the framework regions of certain antibodies can directly participate in antigen binding or can affect the ability of one or more amino acids in CDRs to interact with antigen.

Examples of antibodies are anti PCSK-9 mAb (e.g., Alirocumab), anti IL-6 mAb (e.g., Sarilumab), and anti IL-4 mAb (e.g., Dupilumab).

Further examples of APIs for the prophylaxis of hemophilia A or B, with or without inhibitors, include an siRNA targeting antithrombin. An example of an siRNA targeting antithrombin is fitusiran. The term "prophylaxis" and "prophylactic treatment" are used interchangeably herein

Pharmaceutically acceptable salts of any API described herein are also contemplated for use in a drug or medicament in a drug delivery device. Pharmaceutically acceptable salts are for example acid addition salts and basic salts.

Those of skill in the art will understand that modifications (additions and/or removals) of various components of the APIs, pharmaceutical formulations, apparatuses, methods, systems and embodiments described herein may be made without departing from the full scope and spirit of the present invention, which encompass such modifications and any and all equivalents thereof.

An example drug delivery device may involve a needle-based injection system as described in Table 1 of section 5.2 of ISO 11608-1:2014(E). As described in ISO 11608-1:2014(E), needle-based injection systems may be broadly distinguished into multi-dose container systems and single-dose (with partial or full evacuation) container systems. The container may be a replaceable container or an integrated non-replaceable container.

As further described in ISO 11608-1:2014(E), a multi-dose container system may involve a needle-based injection device with a replaceable container. In such a system, each container holds multiple doses, the size of which may be fixed or variable (pre-set by the user). Another multi-dose container system may involve a needle-based injection device with an integrated non-replaceable container. In such a system, each container holds multiple doses, the size of which may be fixed or variable (pre-set by the user).

As further described in ISO 11608-1:2014(E), a single-dose container system may involve a needle-based injection device with a replaceable container. In one example for such a system, each container holds a single dose, whereby the entire deliverable volume is expelled (full evacuation). In a further example, each container holds a single dose, whereby a portion of the deliverable volume is expelled (partial evacuation). As also described in ISO 11608-1:2014(E), a single-dose container system may involve a needle-based injection device with an integrated non-replaceable container. In one example for such a system, each container holds a single

dose, whereby the entire deliverable volume is expelled (full evacuation). In a further example, each container holds a single dose, whereby a portion of the deliverable volume is expelled (partial evacuation).

Fitusiran as the API for the medicament in the device

Fitusiran is a synthetic, chemically modified double-stranded small interfering RNA (siRNA) oligonucleotide covalently linked to a tri-antennary N-acetyl-galactosamine (GalNAc) ligand targeting AT3 mRNA in the liver, thereby suppressing the synthesis of antithrombin. *See, e.g.*, Pasi et al., *N Engl J Med.* (2017) 377(9):819-28. The nucleosides in each strand of fitusiran are connected through either 3'-5' phosphodiester or phosphorothioate linkages, thus forming the sugar-phosphate backbone of the oligonucleotide.

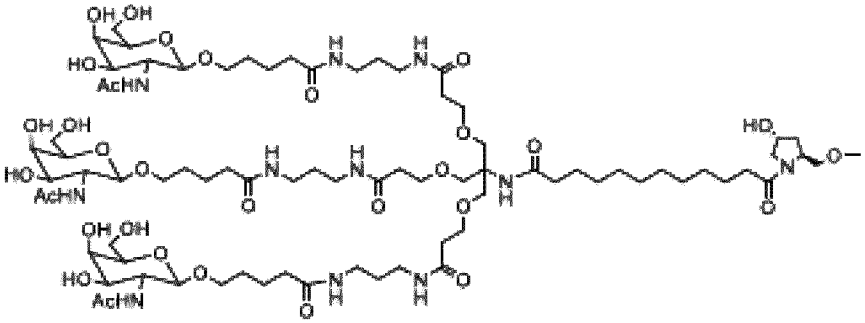
The sense strand and the antisense strand contain 21 and 23 nucleotides, respectively. The 3' end of the sense strand is conjugated to the GalNAc containing moiety (referred to herein as L96) through a phosphodiester linkage. The sense strand contains two consecutive phosphorothioate linkages at its 5' end. The antisense strand contains four phosphorothioate linkages, two at the 3' end and two at the 5' end. The 21 nucleotides of the sense strand hybridize with the complementary 21 nucleotides of the antisense strand, thus forming 21 nucleotide base pairs and a two-base overhang at the 3'-end of the antisense strand. See also U.S. Pat. 9,127,274, U.S. Pat. 11,091,759, US2020/0163987A1, and WO 2019/014187, the entire contents each of which are expressly incorporated herein by reference.

The two nucleotide strands of fitusiran are shown below:
sense strand: 5'Gf-ps-Gm-ps-Uf-Um-Af-Am-Cf-Am-Cf-Cf-Af-Um-Uf-Um-Af-Cm-Uf-Um-Cf-Am-Af-L96 3' (SEQ ID NO:1), and
antisense strand: 5' Um-ps-Uf-ps-Gm-Af-Am-Gf-Um-Af-Am-Af-Um-Gm-Gm-Uf-Gm-Uf-Um-Af-Am-Cf-Cm-ps-Am-ps-Gm 3' (SEQ ID NO:2),
wherein
Af = 2' -deoxy- 2'-fluoroadenosine
Cf = 2' -deoxy- 2'-fluorocytidine
Gf = 2' -deoxy- 2'-fluoroguanosine
Uf = 2' -deoxy- 2'-fluorouridine
Am = 2'-O-methyladenosine
Cm = 2'-O-methylcytidine
Gm = 2'-O-methylguanosine
Um = 2'-O-methyluridine

"-" (hyphen) = 3'-5' phosphodiester linkage sodium salt

"-ps-" = 3'-5' phosphorothioate linkage sodium salt

and wherein L96 has the following formula:



(I).

As used herein, the terms 2' -deoxy- 2'-fluoroadenosine and 2'-fluoroadenosine may be used interchangeably.

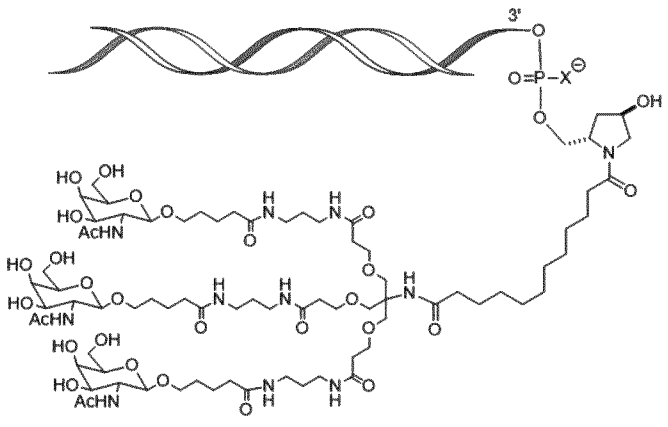
As used herein, the terms 2' -deoxy- 2'-fluorocytidine and 2'-fluorocytidine may be used interchangeably.

As used herein, the terms 2' -deoxy- 2'-fluoroguanosine and 2'-fluoroguanosine may be used interchangeably.

As used herein, the terms 2' -deoxy- 2'-fluorouridine and 2'-fluorouridine may be used interchangeably.

The expanded structural formula, molecular formula, and molecular weight of fitusiran are shown in Figure 4.

The structure of fitusiran can also be described using the following diagram, wherein the X is O:



Fitusiran is shown in Figure 4 in sodium salt form.

In some embodiments, the device delivers fitusiran in an aqueous solution, wherein fitusiran is at a concentration of about 40 to about 200 mg/mL (e.g., about 50 to about 150 mg/mL, about 80 to about 110 mg/mL, or about 90 to about 110 mg/mL). As used herein, values intermediate to recited ranges and values are also intended to be part of this disclosure. In addition, ranges of values using a combination of any of recited values as upper and/or lower limits are intended to be included. In further embodiments, the pharmaceutical formulation comprises fitusiran in an aqueous solution at a concentration of about 40, about 50, about 75, about 100, about 125, about 150, or about 200 mg/mL. In certain embodiments, fitusiran is provided in an aqueous solution at a concentration of about 100 mg/mL.

The term “deliver,” “delivers,” or “delivering” is intended to mean “administer,” “administers,” or “administering.”

Unless specifically stated or otherwise evident from the context, as used herein, the term “approximately” or "about" refers to a value that is within an acceptable error range for a particular value determined by a person of ordinary skill, a portion of which will depend on how the measurement or determination is made. For example, “approximately” or "about" may mean a range of up to 10% (ie, ±10%). Therefore, “approximately” or "about" can be understood as greater than or less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.1 %, 0.05%, 0.01%, or 0.001%. When a specific value is provided in this disclosure, unless otherwise stated, the meaning of “approximately” or "about" should be assumed to be within an acceptable error range for that specific value.

While the fitusiran dosage weight described herein refers to the weight of fitusiran free acid (active moiety), administration of fitusiran to patients herein refers to administration of fitusiran sodium (drug substance) provided in a pharmaceutically suitable aqueous solution (e.g., a phosphate-buffered saline at a physiological pH). For example, about 100 mg/mL fitusiran means about 100 mg of fitusiran free acid (equivalent to about 106 mg fitusiran sodium, the drug substance) per mL. Unless otherwise indicated, a fitusiran weight recited in the present disclosure is the weight of fitusiran free acid (the active moiety).

In some embodiments, a pharmaceutical formulation in the device comprises fitusiran in a phosphate-buffered saline. The phosphate concentration in the solution may be about 1 to about 10 mM (e.g., about 2, about 3, about 4, about 5, about 6, about 7, about 8, or about 9 mM), with a pH of about 6.0-8.0. The pharmaceutical formulations herein may include a

stabilizing agent such as EDTA. The pharmaceutical formulations may be preservative-free. In some embodiments, the fitusiran pharmaceutical formulation in the device is preservative-free and comprises, consists of, or consists essentially of about 100 mg of fitusiran per mL of an approximately 5 mM phosphate buffered saline (PBS) solution. In some embodiments, the fitusiran pharmaceutical formulation in the device is preservative-free and comprises, consists of, or consists essentially of fitusiran in an approximately 5 mM phosphate buffered saline (PBS) solution. The PBS solution is composed of sodium chloride, dibasic sodium phosphate (heptahydrate), and monobasic sodium phosphate (monohydrate). Sodium hydroxide solution and diluted phosphoric acid may be used to adjust the pH of the pharmaceutical formulation to about 7.0 or about 7.1.

In some embodiments, the fitusiran pharmaceutical formulation in the device for subcutaneous delivery contains fitusiran in a 5 mM phosphate buffered saline having 0.64 mM NaH_2PO_4, 4.36 mM Na_2HPO_4, and 84 mM NaCl at pH 7.0. In certain embodiments, the pharmaceutical formulation of fitusiran solution for subcutaneous delivery is shown in **Table 1** below:

Table 1. Exemplary Fitusiran Pharmaceutical Formulation

Components	**Pharmaceutical Formulation**	
	Percentage [%]	Per ml [mg]
Fitusiran (active moiety) [equivalent to fitusiran sodium]	10	100 [106]
Sodium chloride	0.49	4.909
Dibasic sodium phosphate (heptahydrate)	0.12	1.169
Monobasic sodium phosphate (monohydrate)	<0.01	0.0885
Phosphoric acid, concentrated	-	q.s. pH 7.0
Sodium hydroxide	-	q.s. pH 7.0
Water for subcutaneous delivery	q.s. 100	q.s. 1 mL

*q.s.: quantum satis

In some embodiments, the pharmaceutical formulation of fitusiran solution for subcutaneous delivery with the device can be described as shown in **Table 2** below.

Table 2. Exemplary Fitusiran Pharmaceutical Formulation

Components	Pharmaceutical Formulation (mg)
Fitusiran (active moiety) [equivalent to fitusiran sodium]	100 [106]
$NaH_2PO_4*H_2O$	0.0885
$Na_2HPO_4*7H_2O$	1.169
NaCl	4.909
0.1 N NaOH	q.s.
0.1 M H_3PO_4	q.s.
Purified water	*Ad* 1 mL

In some embodiments, the device may be used to deliver a single dose of fitusiran wherein the single dose comprises about 20 to about 80 mg of fitusiran (e.g., about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, or about 80 mg). In some embodiments, the device may be used to deliver single dose of fitusiran, wherein the single dose comprises about 1 to about 30 mg of fitusiran (e.g., about 1.25 mg, about 2.5 mg, about 5 mg, about 10 mg, about 20 mg, or about 30 mg).

In one embodiment, the device may be used to deliver a single dose of about 80 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 50 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 20 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 30 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 10 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 5 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 2.5 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 1.25 mg of fitusiran.

In some embodiments, the single dose of fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL). Other delivery volumes described herein may also be used.

In one embodiment, the device may be used to deliver a single dose of about 80 mg of fitusiran in about 0.8 mL (about 100 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 50 mg of fitusiran in about 0.5 mL (about 100 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 20 mg of fitusiran in about 0.5 mL (about 40 mg fitusiran/mL). In one embodiment, the device may be used to

deliver a single dose of about 30 mg of fitusiran in about 0.5 mL (about 60 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 10 mg of fitusiran in about 0.5 mL (about 20 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 5 mg of fitusiran in about 0.5 mL (about 10 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 2.5 mg of fitusiran in about 0.5 mL (about 5 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 1.25 mg of fitusiran in about 0.5 mL (about 2.5 mg fitusiran/mL).

In one embodiment, the device delivers fitusiran at a prophylactically effective amount to prophylactically treat hemophilia (e.g., hemophilia A or B, in a patient with or without inhibitors) in a patient in need thereof (e.g., a hemophilia A or B patient, with or without inhibitors). "Prophylactically effective amount" refers to the amount of fitusiran that helps the patient with hemophilia A or B, with or without inhibitors to achieve a desired clinical endpoint such as reducing the Annualized Bleeding Rate (ABR), Annualized Joint Bleeding Rate (AjBR), Annualized Spontaneous Bleeding Rate (AsBR), or the frequency of bleeding episodes. As used herein in the context of fitusiran, the term "treat" "treating," or "treatment" includes prophylactic treatment of the disease and refers to achievement of a desired clinical endpoint.

A hemophilia A or B patient with inhibitors refers to a patient who has developed alloantibodies to the factor he/she has previously received (e.g., factor VIII for hemophilia A patients or factor IX for hemophilia B patients). A hemophilia A or B patient with inhibitors may become refractory to replacement coagulation factor therapies. A patient without inhibitors refers to a patient who does not have such alloantibodies. The present treatment methods may be beneficial for hemophilia A patients with inhibitors, as well as for hemophilia B patients with inhibitors.

As used herein, a patient with "hemophilia A or B, with or without inhibitors," or refers to 1) a hemophilia A patient with inhibitors, or 2) a hemophilia B patient with inhibitors, 3) a hemophilia A patient without inhibitors, or 4) a hemophilia B patient without inhibitors. As used herein, a patient refers to a human patient. A patient can also refer to a human subject.

In some embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 50 mg of fitusiran once every two months (or every eight weeks). In other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 50 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 80 mg of fitusiran every two

months (or every eight weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 80 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 20 mg of fitusiran every two months (or every eight weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 20 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 10 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 30 mg every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 5 mg every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 2.5 mg every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 1.25 mg every month (or every four weeks).

Accordingly, provided herein is a method of prophylactic treatment of a patient with hemophilia A or hemophilia B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of prophylactic treatment of a patient with hemophilia A or hemophilia B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Further provided herein is a method of reducing the frequency of bleeding episodes in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the frequency of bleeding episodes in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Also, provided herein is a method of reducing the ABR in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the ABR in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Also, provided herein is a method of reducing the AjBR in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically

effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). The fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the AjBR in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Also, provided herein is a method of reducing the AsBR in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the AsBR in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Any invention described herein is not limited by the description in conjunction with the exemplary embodiments. Rather, the invention and the associated disclosure comprise any new feature as well as any combination of features, particularly including any combination of features in the patent claims, even if said feature or said combination per se is not explicitly stated in the patent claims or exemplary embodiments.

Reference numerals

drug delivery device	1
housing unit	2
drug delivery arrangement	3
arrangement housing	4
medicament container	5
needle	6
plunger rod	7
drive energy source	8
stopper	9
cap	10
needle shield remover	11
needle shield	12
needle shroud	13
shroud spring	14
receiving chamber	15
opening	16
stop surface	17
fixation member	18
mechanical lock	19
guide rod	20
proximal guiding member	21
distal guiding member	22
container carrier	23
first shroud position	A
second shroud position	B
third shroud position	C

Claims

1. A drug delivery device (1) comprising
a housing unit (2), and
at least two drug delivery arrangements (3), each having
a drive energy source (8) for providing energy for a drug delivery operation,
a medicament container (5) for receiving a drug, and
a needle (6), being associated with the respective medicament container,
wherein the at least two drug delivery arrangements are positioned in the housing unit, such that the medicament containers are fluidically separated with respect to each other.

2. The drug delivery device (1) according to claim 1, wherein the drug delivery device is configured such that the energy of the drive energy sources (8) of the two drug delivery arrangements (3) can be released simultaneously in order to dispense the drugs simultaneously.

3. The drug delivery device (1) according to claim 1, wherein the drug delivery device is configured such that the energy of the drive energy sources (8) of the two drug delivery arrangements (3) can be released at different times in order to dispense the drugs at different times.

4. The drug delivery device (1) according to any of the preceding claims, wherein the drug delivery device is configured such that the distance between the respective distal tip of the needle (6) and the distal end of the housing unit (2) is the same during a drug delivery operation.

5. The drug delivery device (1) according to any of the claims 1-3, wherein the drug delivery device is configured such that the distances between the distal tips of the needles (6) and the distal end of the housing unit (2) are different to each other during a drug delivery operation.

6. The drug delivery device (1) according to any of the preceding claims wherein each of the drug delivery arrangements (3) is configured to perform a drug delivery operation by releasing the respective energy of the drive energy source (8) in order to dispense the drug when the respective drug delivery arrangement is positioned in the housing unit (2) and when the respective drug delivery arrangement is separated from the housing unit.

7. The drug delivery device (1) according to any of the preceding claims, wherein the housing unit (2) comprises at least two receiving chambers (15), wherein each of the receiving chambers is configured to receive and axially secure one of the two drug delivery arrangements (3) in a repeatedly removable manner, and
wherein the two receiving chambers are configured such that the drug delivery device is able to perform the drug delivery operation regardless of in which of the two chambers the respective drug delivery arrangement is received and secured in.

8. The drug delivery device (1) according to claim 7, wherein each of the receiving chambers (15) is closed in the proximal end region of the respective receiving chamber and has an opening (16) in the distal end region of the respective receiving chamber, wherein the opening is configured to allow the drug delivery arrangement (3) to be inserted into the receiving chamber through the opening,
wherein the respective closed proximal end region provides a stop surface (17) to prevent the drug delivery arrangement against further movement in the proximal direction after the drug delivery arrangement is received by the receiving chamber, and
wherein at least one of the two receiving chambers has a distal end region in which the inner diameter decreases continuously in the proximal direction to facilitate insertion of the respective drug delivery arrangement.

9. The drug delivery device (1) according to claim 7 or 8, wherein at least one of the receiving chambers (15) comprises at least one fixation member (18) for fixating the respective drug delivery arrangement (3) in the receiving chamber,
wherein the drug delivery arrangement has at least one recess providing a window, and
wherein the fixation member comprises a protrusion configured to engage the recess of the window in order to lock the drug delivery arrangement in the receiving chamber against distal, proximal and rotational movement relative to the housing unit (2).

10. The drug delivery device (1) according to claim 7 or 8, wherein at least one of the receiving chambers (15) comprises two fixation members (18) which are spaced axially offset from each other by more than half the length of the receiving chamber along the inner circumferential surface of the receiving chamber.

11. The drug delivery device (1) according to claim 10, wherein the respective fixation member (18) is an O-shaped ring.

12. The drug delivery device (1) according to any of the claims 8-11, wherein each of the drug delivery arrangements (3) has an arrangement housing (4) and a cap (10) connected to the respective arrangement housing, and
wherein at least one of the receiving chambers (15) is configured such that, when the respective drug delivery arrangement is secured in the receiving chamber, the cap protrudes at least sufficiently from the opening (16) to allow a user to grasp the cap in order to separate the cap from the arrangement housing.

13. The drug delivery device (1) according to claim 12, wherein the radial distance between the central longitudinal axes of the two receiving chambers (15) is greater than the diameter of the respective drug delivery arrangement (3) with the cap (10) at its largest position.

14. The drug delivery device (1) according to any of the claims 1-5, wherein the drug delivery device comprises a needle shroud (14), configured to enclose both of the two needles (6),
wherein the needle shroud is axially movable relative to the needles, and
wherein the drug delivery device is configured such that the release of the energy of both drive energy sources (8) is triggered by a movement of the needle shroud relative to the needles.

15. The drug delivery device (1) according to any of the claims 1-5 and 14, wherein the drug delivery device comprises a cap (10), configured to cover the distal end portions of both of the two medicament containers (5).

16. The drug delivery device (1) according to any of the preceding claims, wherein the drug delivery device is configured such that the distances between the distal tips of the needles (6) and the distal end of the housing unit (2) are different to each other during a drug delivery operation, such that the tips of the needles protrude from the housing unit to different extents or by different distances, after the energies of the drive energy sources (8) of the two drug delivery arrangements (3) have been released.

17. The drug delivery device (1) according to any of the preceding claims, wherein the drug delivery device is configured such that the distances between the distal tips of the needles (6) and the distal end of the housing unit (2) are different to each other prior to a drug delivery operation, such that the tips of the needles protrude from the housing unit

to different extents or by different distances, before the energies of the drive energy sources (8) of the two drug delivery arrangements (3) have been released.

18. The drug delivery device (1) according to any of the preceding claims, wherein the drug delivery device further comprises a needle shroud (13), wherein the needle shroud is configured:
- to be axially movable relative to the housing unit (2) between an initial position (A) and a final position (C),
- to cover the respective needle (6) by extending axially beyond the tip of the needle in the distal direction in both the initial position and the final position, and
- to extend further in the distal direction in the final position than in the initial position.

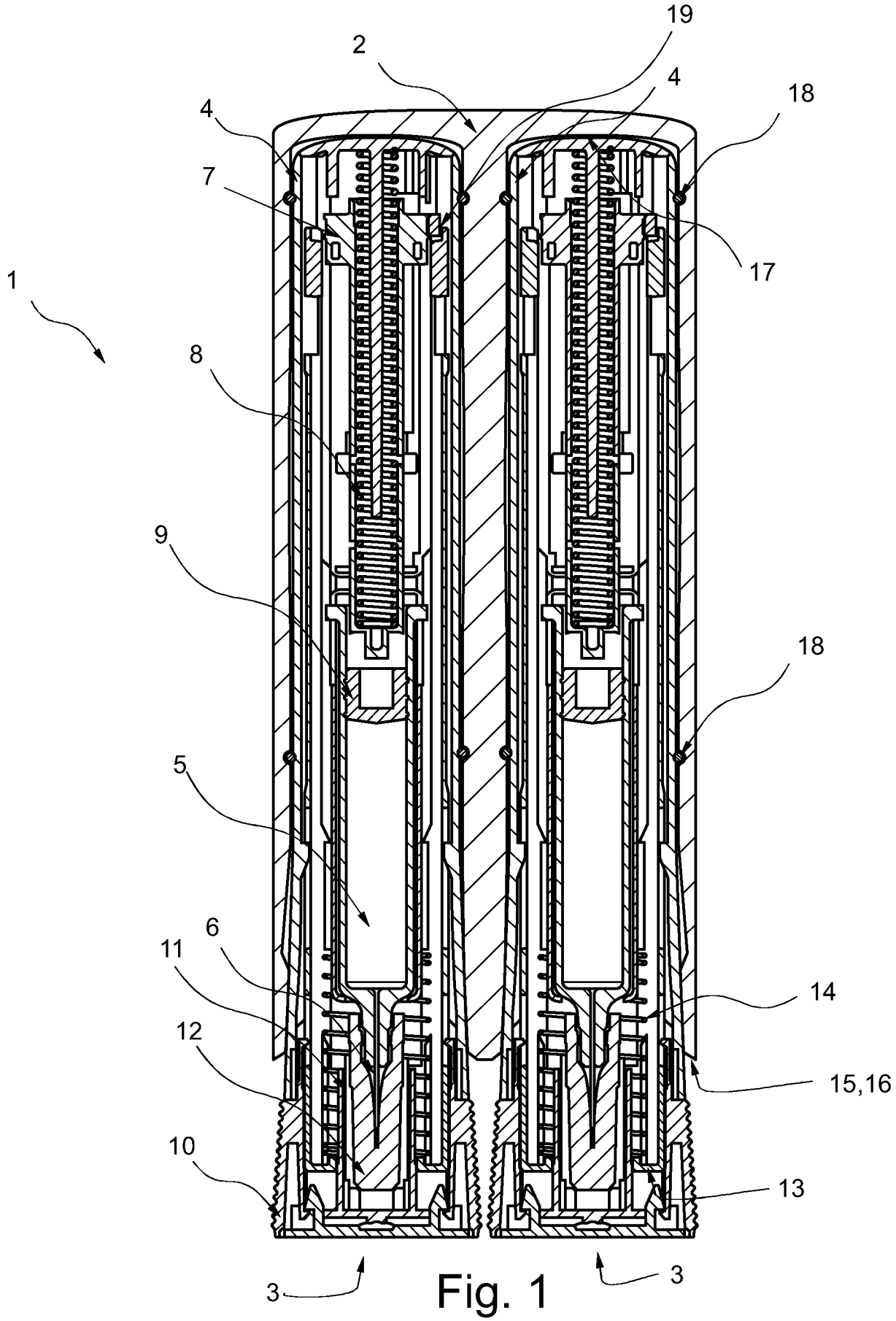


Fig. 1

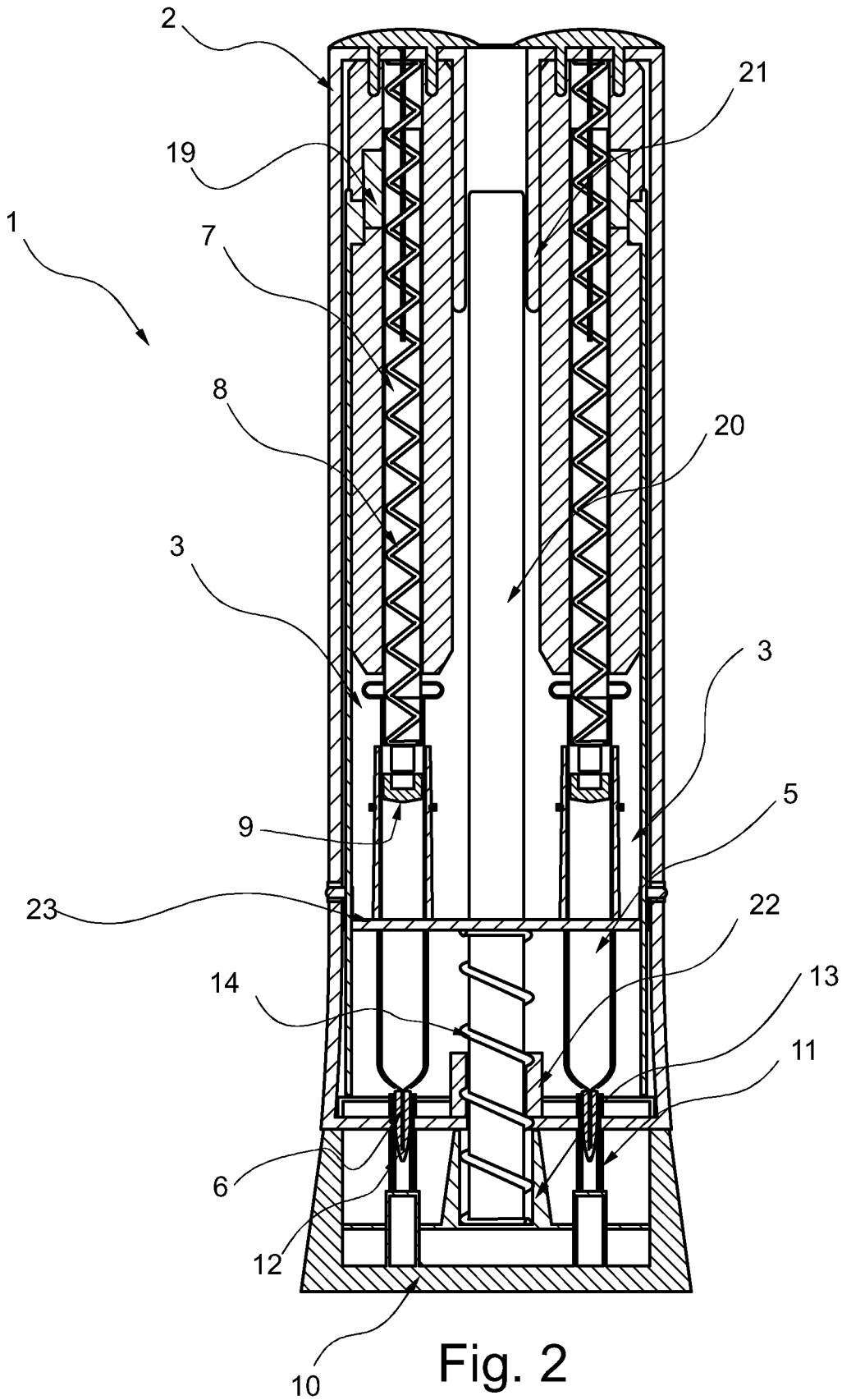


Fig. 2

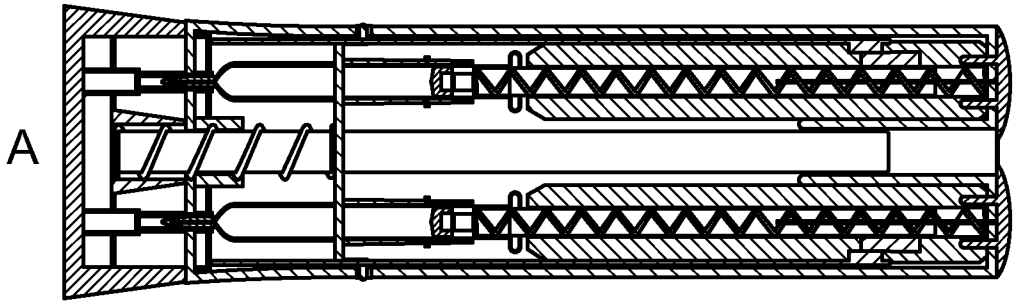


Fig. 3A

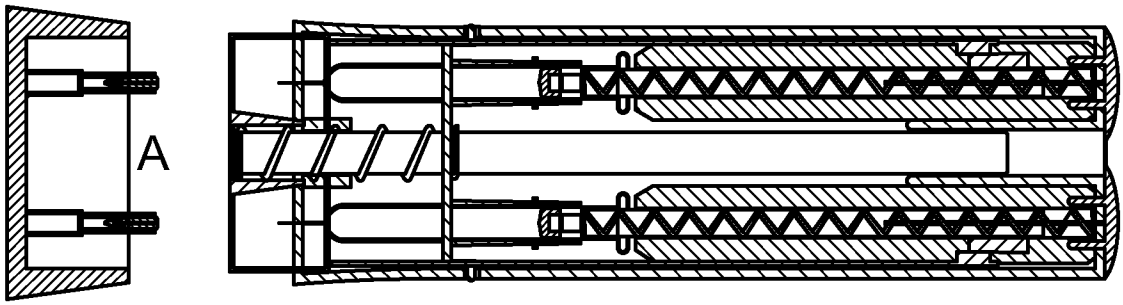


Fig. 3B

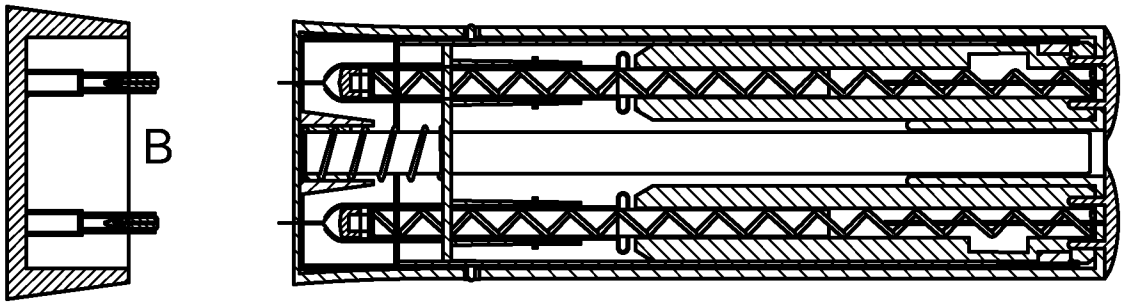


Fig. 3C

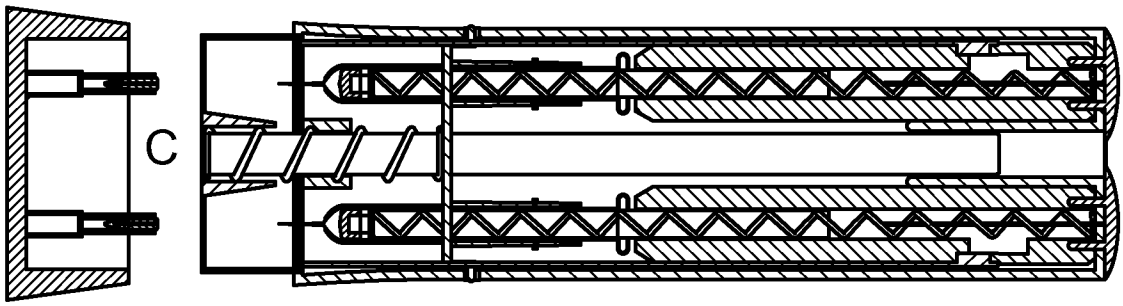
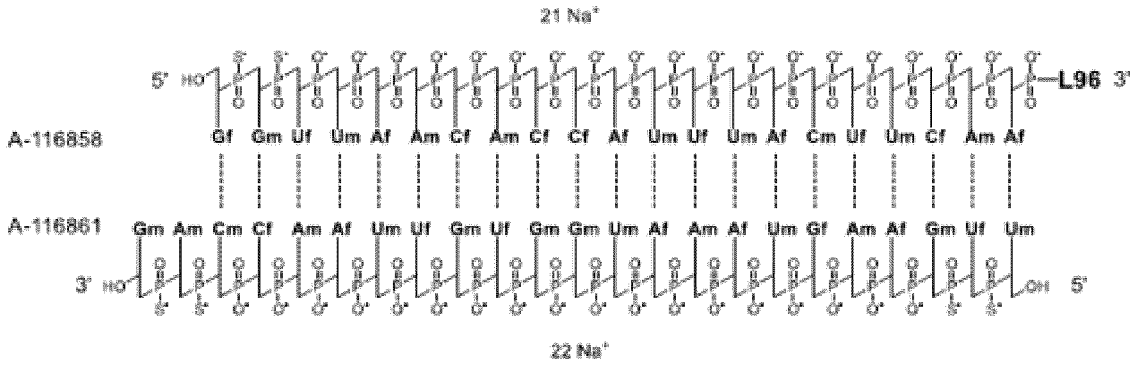
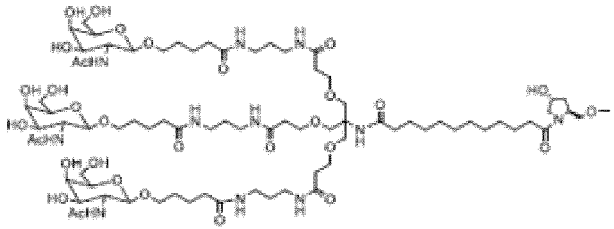


Fig. 3D



Af, Cf, Gf, Uf = 2'-F ribonucleosides
Am, Cm, Gm, Um = 2'-OMe ribonucleosides

L96 =



Molecular formula and molecular mass

	Fitusiran (Duplex)	A-116858 (Sense strand)	A-116861 (Antisense strand)
Molecular formula sodium salt	$C_{520}H_{636}F_{21}N_{175}Na_{43}O_{309}P_{43}S_6$	$C_{285}H_{369}F_{12}N_{65}Na_{21}O_{164}P_{21}S_2$	$C_{235}H_{267}F_9N_{90}Na_{22}O_{145}P_{22}S_4$
Molecular formula free acid	$C_{520}H_{675}F_{21}N_{175}O_{309}P_{43}S_6$	$C_{285}H_{390}F_{12}N_{65}O_{164}P_{21}S_2$	$C_{235}H_{289}F_9N_{90}O_{145}P_{22}S_4$
Molecular weight sodium salt	17,193 Da	9,035 Da	8,159 Da
Molecular weight free acid	16,248 Da	8,573 Da	7,675 Da

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/065440

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/19 A61M5/20 A61M5/32
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2022/055839 A1 (EMERGENT PRODUCT DEV GAITHERSBURG INC [US]) 17 March 2022 (2022-03-17)	1-7, 12-18
A	figures 1, 2, 3, 6A-B, 11A-F, 12 paragraphs [0030] - [0084]	8-11
X	EP 0 014 006 A2 (SURVIVAL TECHNOLOGY [US]) 6 August 1980 (1980-08-06)	1-10, 12-17
A	figures 1, 2, 3, 4, 5, 6, 7, 8 page 11, line 1 - page 33, line 17	11,18
A	WO 2014/205604 A1 (C C BIOTECHNOLOGY CORP [CN] ET AL.) 31 December 2014 (2014-12-31) the whole document	1-15

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 September 2024	23/09/2024

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Benes, Václav

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2024/065440

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed.

   b. ☒ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

      ☒ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2024/065440

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		WO 2014205604 A1	31-12-2014