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# (54) Title: RIBOZYME BASED TREATMENT OF FEMALE REPRODUCTIVE DISEASES

(57) Abstract: The present invention relates to nucleic acid molecules, including dsRNA, siRNA, antisense, 2,5-A chimeras, aptamers, and enzymatic nucleic acid molecules, such as hammerhead ribozymes, DNAzymes, and allozymes, which modulate the expression of vascular endothelial growth factor receptor (VEGF) and/or vascular endothelial growth factor receptor (VEGFr) genes for the treatment and/or diagnosis of diseases and conditions associated with angiogenesis, such as cancer, tumor angiogenesis, or ocular indications such as diabetic retinopathy, or age related macular degeneration, proliferative diabetic retinopathy, hypoxia-induced angiogenesis, rheumatoid arthritis, psoriasis, wound healing, and female reproductive disorders and conditions, including but not limited to endometriosis, endometrial carcinoma, gynecologic bleeding disorders, irregular menstrual cycles, ovulation, premenstrual syndrome (PMS), and menopausal dysfunction.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/17674

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| A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) : C07H 21/04; C12Q 1/68; C12N 5/00  US CL : 514/44; 536/24.5, 435/6, 91.31, 375                                |   |   |   |  |
| According to International Patent Classification (IPC) or to both national classification and IPC  B. FIELDS SEARCHED                                      |   |   |   |  |
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| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched                              |   |   |   |  |
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| C. DOCUMENTS CONSIDERED TO BE RELEVANT   |   |   |   |  |
| Category *   | Citation of document, with indication, where ap   |   | Relevant to claim No.   |  |
| Y  | PARRY, T.J. et al. Bioactivity of anti-angiogenic ribozymes targeting F1t-1 and KDR mRNA, Nucleic Acids Research, 1999, Vol. 27, No.13, pages 2569-2577, see entire document. |   | 1-2   |  |
| Α  |   |   | 3-103   |  |
| A WO 99/04819 A1 (INEX PHARMACEUTICALS, (04.02.1999), see entire document.   |   | CORP.) 04 February 1999   | 1-51, 54-103  |  |
| (04.02.1999), see entire document.   |   |   | 52-53   |  |
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