

Hope Medicine

Category:

Best Startup

Company Name:

Hope Medicine

Turnover and/or Funding:

HopeMed raised more than 90 million USD through three funding rounds (A, B and B+). Major investors include Qiming, Grand Flight and Trustbridge.

Sub-Category:

Biotechnology

Corporate history (creation, key milestones, main funding,...) Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

Hope Medicine (HopeMed) was founded in 2018 by Professor Rui Ping Xiao of Peking University in China. Professor Xiao had worked in NIH as a tenured senior investigator for more than two decades before she joined Peking University and founded the Institute of Molecular Medicine more than 10 years ago. In 2019, HopeMed in-licensed HMI-115, a potential first-in-class treatment for endometriosis, from Bayer, who entrusted its global development to Professor Xiao because of their excellent collaboration and her reputation. This is the only time that Bayer, during its 150 years history, out-licensed global rights to a Chinese biotech. The CEO, Nathan Chen, joined HopeMed in 2023 with 29 years' experience in US, China and Singapore, successfully leading clinical development of FIC assets like mavacamten, belimumab, and dabigatran. The President, Damian Tu, joined HopeMed in 2020 with 15 years' experience in US and China focusing on manufacturing blockbusters like Humira and Skyrizi.

Endometriosis is an inflammatory condition marked anatomically by the presence of endometrium-like tissue outside the uterus. Affecting 6%-10% of reproductive-age women and up to 50% of infertile women, endometriosis is one of the most common gynecological conditions. It is estimated that currently at least 190 million women and adolescent girls worldwide are affected by the disease. The primary clinical symptoms include dysmenorrhea, non-menstrual pelvic pain, and dyspareunia. Endometriosis frequently coexists with conditions such as migraine, anxiety, depression, and chronic

fatigue syndrome, which impair the patients' quality of life, fertility, emotional health, and quality of work life, resulting in an average loss of 10.8 hours of work per week. In US, the annual medical cost of endometriosis-associated symptoms is approximately 4,000 USD per patient, which is comparable to that of chronic diseases such as type 2 diabetes mellitus, Crohn's disease, and rheumatoid arthritis, resulting in a significant burden on health resources.

There is currently no cure for endometriosis. The primary objectives of treatment are to relieve pain, reduce recurrence, and to enhance fertility. The treatments include surgery and medication. Excision of all lesions through surgery is often unattainable, resulting in recurrence. Pharmacological treatments include non-steroidal anti-inflammatory drugs (NSAIDs) and hormonal therapies including combined oral contraceptives (COCs), progestins, gonadotropin-releasing hormone (GnRH) agonists and antagonists. While NSAIDs may temporarily alleviate pain, they cannot reduce recurrence and have gastrointestinal side effects. Hormonal therapies relieve pain by inhibiting the hypothalamic-pituitary-ovarian axis (HPO), thereby suppressing ovulation, resulting in a temporary infertility which presents difficulties to endometriosis patients predominantly of child-bearing age. In addition, GnRH agonists and antagonists suppress estrogen and cause perimenopausal symptoms such as depression, bone loss, hot flush and sweating. Progestins and COC are not effective in approximately 1/4 to 1/3 of patients. They also cause breakthrough bleeding, depression, distending pain in breast, weight gain, and thromboembolism.

Consequently, there is an unmet clinical need for a long-term therapy that is both safe and effective while also preserving the integrity of the HPO axis and fertility.

History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):

HMI-115 is a first-in-class investigational monoclonal antibody that blocks the prolactin receptor (PRLR). Prolactin (PRL) has anti-apoptotic and proliferative activity in endometrial cells in the peritoneal cavity of endometriosis patients. PRL and its receptor were found overexpressed in endometriotic lesions compared to eutopic endometrium of patients and healthy controls in in-house studies, suggesting that local autocrine PRL signaling may play a fundamental role in the establishment, growth, and maintenance of endometriotic lesions.

In a murine endometriosis interna model, the antibody demonstrated comparable efficacy to proven endometriosis treatments such as an antiestrogen. In vitro pharmacology studies demonstrated that HMI-115 binds the prolactin receptor and inhibits the proliferation of prolactin-stimulated cells stably transfected with murine and monkey receptors. A tissue cross reactivity study indicated comparable cross-reactivity across human, mice and cynomolgus monkey. Repeat weekly-dose general toxicology studies in mice (13-week) and cynomolgus monkeys (26-week), a fertility study in female monkeys, and a local tolerance study in rabbits were conducted. HMI-115 demonstrated very good tolerability on vital organ functions. No biologically relevant

effects on behavior, body temperature, arterial blood pressure, heart rate, respiratory frequency, or minute volume were observed up to the highest dose tested. The fertility study in female cynomolgus monkeys showed that HMI-115 did not affect the mating and gestation, indicating its potential safety in women of childbearing age and its difference from current hormonal treatments, which suppress fertility.

Four clinical studies of HMI-115 are completed. Study 16288 was a FIH Phase 1 PK study of subcutaneous administration to healthy postmenopausal women (N=100) in Germany. Study HMI-115102 was a Phase 1b study in males and females (N=16) with androgenic alopecia with a 24-week treatment period in Australia. Study HMI-115EM201 is a Phase 2 study for moderate to severe endometriosis-associated pain with a 12-week treatment period in patients (N=142) from the US, Poland, and China. Study HMI-115AG201 is a Phase 2 study for androgenetic alopecia with a 24-week treatment period in male patients (N=193) from China. In these four completed clinical studies, HMI-115 was safe and well-tolerated in over 300 subjects up to 240 mg Q2W for 24 weeks. There were no deaths or drug related SAEs. Most adverse events (AEs) were mild or moderate in severity.

Study HMI-115EM201 provided proof-of-concept that PRL blockade can treat endometriosis associated pain. It demonstrated significant reduction of dysmenorrhea by 42% ($p=0.036$) and non-menstrual pelvic pain by 52% ($p=0.042$) in the 240 mg q2w group compared to placebo, consistent between Asian and Caucasians. In the 240 mg q2w group, rescue analgesics was reduced by 70%, and up to 70% patients reported their symptoms much improved or very much improved. Almost all patients had normal menstruation. There were no significant changes in the average menstrual cycle durations, and in sex hormones (Estradiol, FSH, LH, progesterone), indicating that patients may have normal ovulation during the treatment. There were no typical peri-menopausal symptoms (bone loss, depression, hot flush, sweating). The break-through findings of this study pave the path towards a long-awaited paradigm-shifting non-hormonal treatment of endometriosis.

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:

HMI-115 can potentially improve women's health worldwide by addressing a critical clinical need for a long-term therapy that is safe and effective while also preserving the integrity of the hypothalamic-pituitary-ovarian axis (HPO) and fertility. HMI-115 is a first-in-class treatment of endometriosis by blocking the prolactin receptor (PRLR). It is the first non-hormonal treatment that passed proof-of-concept.

The primary objectives of endometriosis treatment are to relieve pain, reduce recurrence, and to enhance fertility. The standard of care includes both surgery and medications. The limitation of surgery is recurrence since complete excision of all lesions is often unattainable. The 2-year recurrence rate after endometriosis surgery is 21.5%, and the 5-year recurrence rate is 40-50%. Surgery also carries risk of complications.

Medications for endometriosis and endometriosis-associated pain include non-steroidal

anti-inflammatory drugs (NSAIDs), combined oral contraceptives (COCs), progestins, gonadotropin-releasing hormone (GnRH) agonists and antagonists. While NSAIDs is non-hormonal by nature and may provide limited temporary pain reduction, they cannot prevent recurrence and have gastrointestinal side effects.

The current hormonal therapies inhibit HPO, thereby suppressing ovulation, resulting in a temporary infertility during treatment which presents difficulties to endometriosis patients since they are predominantly of child-bearing age. Endometriosis can cause infertility, and many patients get diagnosed because they have experienced difficulties getting pregnant. It is disheartening to tell a patient already in doubt of her fertility that she still cannot get pregnant while on her hormonal treatment, and that she will need to pause her hormonal therapy and try pregnancy before the pain comes back, often within 1 to 2 months. This causes significant mental stress which further complicates gestation. HMI-115, in contrast, can relieve a patient from such stress since it does not impact HPO or inhibit ovulation. Treatment with HMI-115 did not lead to significant changes in patients' menstrual patterns or key sex hormones, indicating normal ovulation on treatment. In line with these observations, a monkey fertility study indicates that HMI-115 up to 50 mg/kg did not interfere with mating and gestation. In addition, HMI-115 does not cause the troublesome side effects associated with the hormonal treatments since it does not suppress estrogen or over-stimulate progesterone. GnRH agonists and antagonists suppress estrogen thus causing perimenopausal symptoms, and their long-term uses may cause bone loss, which limit their duration of treatment to 6 months or 2 years. In contrast, HMI-115 improved symptoms of endometriosis without affecting sex hormones and thus was devoid of hypoestrogenic symptoms, such as depression, bone loss, sweating and hot flush, allowing long-term treatment.

Progestins can cause side effects such as breakthrough bleeding, depression, distending pain in breast, fluid retention, gastrointestinal symptoms, and abnormal hepatic functions. COCs can cause weight gain, hepatic impairment, thromboembolism, and an increased risk of breast cancer. Notably, 1/4 to 1/3 of patients do not respond to COC or progestins. HMI-115 does not change progesterone therefore is devoid of the above side effects that dampen the acceptance of progestins and COCs.

Beyond pain relief, HMI-115 can be disease-modifying since it cleared lesions in a murine endometriosis interna model.

Please provide appropriate references (PubMed, Abstract, Website):

Rüdiger, N et al; Monoclonal Antibody Against Prolactin Receptor: A Randomized Placebo-Controlled Study Evaluating Safety, Tolerability, and Pharmacokinetics of Repeated Subcutaneous Administrations in Postmenopausal Women; Reprod Sci. 2019 Apr;26(4):523-531.

A Randomized, Multicenter, Double-Blind, Placebo-Controlled Phase 2 Study to Evaluate the Safety and Efficacy of HMI-115 in Women with Moderate to Severe Endometriosis-Associated Pain Over a 12-Week Treatment Period [CONFIDENTIAL

STUDY REPORT]

Zhu, L et al; Efficacy and Safety of Subcutaneous Injection with HMI-115 versus Placebo in Endometriosis-Associated Pain: a Multicenter, Double-blind, Randomized, Proof-of-concept Phase 2 Trial; The Lancet Obstetrics, Gynaecology, & Women's Health [ACCEPTED AND TO BE PUBLISHED]

Wang, R et al; Single-cell RNA sequencing identifies the prolactin receptor as a therapeutic target in adenomyosis; Sig Transduct Target Ther 10, 258 (2025)

References File Document upload:

N/A