BIOBUSINESS BRIEFS

DEAL WATCH

Abbott and Neurocrine to develop promising endometriosis drug

Abbott and Neurocrine Biosciences have entered into a collaboration to develop and commercialize elagolix, a gonadotropin-releasing hormone (GnRH) antagonist that has recently completed a Phase IIb study in patients with endometriosis, a condition in which cells that normally line the womb proliferate pathologically outside the uterus. The potential advantages of elagolix over existing treatments could include oral administration and a more rapid onset of therapeutic action.

Under the terms of the agreement, Abbott receives worldwide exclusive rights to develop and to commercialize elagolix and all next-generation GnRH antagonists. In return, Neurocrine receives an upfront payment of US$75 million and funding for all ongoing development activities. Neurocrine is eligible to receive additional payments of approximately $500 million for the achievement of development, regulatory and commercial milestones, and royalty payments on future product sales.

"The primary symptom of endometriosis that requires treatment is pelvic pain with multiple characteristics, including dysmenorrhoea (pain during menstruation), dyspareunia (pain during intercourse), dyschezia (difficulty in defecating) and dysuria (painful urination)," explains David Adamson, Director of Fertility Physicians of Northern California at San Jose and Palo Alto, California, USA. "Current treatments for the condition include GnRH agonists, which are effective in many, but not all, patients with endometriosis-associated pelvic pain."

GnRH agonists achieve their effect in endometriosis by the suppression of oestrogen. Chronic administration of a GnRH agonist, after initial stimulation, reversibly shuts down the secretion of pituitary hormones that are responsible for oestrogen production through desensitization of the GnRH signalling system. As endometriosis tissue growth is reliant on oestrogen this leads to atrophy of the tissue. By directly antagonizing the GnRH receptor with compounds such as elagolix, the initial stimulation observed with agonists of the receptor would not occur.

"A potential advantage of GnRH antagonists lies in the fact they immediately create a hypoestrogenic state when their use is started, as opposed to the ~10–14 days it takes for GnRH agonists to result in ovarian suppression," says Adamson. "This characteristic of GnRH antagonists raises the possibility of intermittent treatment for endometriosis, thereby allowing longer and safer use of the drug with fewer side effects. However, the effectiveness of such strategies in achieving this is yet to be demonstrated."

In addition, as Tommaso Falcone, Professor and Chair of Obstetrics, Gynaecology and Women's Health at the Cleveland Clinic, Ohio, USA, notes: "In contrast to currently used peptidic GnRH agonists that are administered by injection or nasal spray, elagolix is not a peptide and can therefore be orally administered, which could be preferable for patients."

In the recent clinical trial of 137 individuals with endometriosis, in which subjects received 150 mg of elagolix or placebo once daily for 2 months of treatment, top-line results showed that primary and secondary end points were met. Reductions in dysmenorrhoea, non-menstrual pelvic pain and dyspareunia following elagolix administration were seen when compared with placebo. A responder analysis — defined as clinically meaningful if there was an improvement of 30% or greater from baseline — also showed reductions in the three symptoms. However, "although overall these results were positive, there were a large number of non-responders and a relatively high placebo rate of 33%," cautions Falcone.

Both Adamson and Falcone note that because GnRH antagonists and agonists work to suppress gonadotropin, they will probably both have similar clinical efficacy, and perhaps also some of the same side effects, such as hypoestrogenism that can result in bone density loss and other menopausal-like symptoms. "The ultimate drug for endometriosis would be one that acted directly on the endometriosis tissue, rather than by simply suppressing an endogenous hormone such as oestrogen," concludes Falcone.