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GlobalData
OpportunityAnalyzer

ENDOMETRIOSIS - OPPORTUNITY ANALYSIS AND FORECASTS TO 2017

Executive Summary

The table below presents the key metrics for endometriosis therapeutics in the six major pharmaceutical markets covered in this report (US, France, Germany, Italy, Spain, and UK) during the forecast period from 2012–2017. For the purposes of this report, the endometriosis market consists of drugs commonly prescribed to patients with a diagnosis of endometriosis confirmed by laparoscopy. While certain classes of drugs commonly used off label — namely, combined oral contraceptives (COCs) — which contain both an estrogen and a progestin — are included in this forecast, others are not. For example, non-steroidal anti-inflammatory drugs (NSAIDs) and other analgesics are deliberately omitted from this analysis.

Endometriosis Therapeutics: Key Metrics in Six Major Markets (6MM), 2012–2017	
2012 Patient Population 6MM	
Prevalent population (ages 15–19 Years)	5.8 million
Prevalent population (ages 20–49 Years)	8.3 million
Treated population*	
2012 Market Sales	
US	1.64 billion
5EU	71.1 million
Total	**1.71 billion**
Key Events (2012–2017)	**Level of Impact**
Lupron (leuprolide acetate) patent expiry in the US and EU 2014	↓↓
Elagolix launch in the US and EU – 2016	↑↑
2017 Market Sales	
US	$1.67 billion
5EU	$68.48 million
Total	**$1.74 billion**

Source: GlobalData
*Excludes patients managed only via NSAIDs or surgery alone.
6MM = US and 5EU (France, Germany, Italy, Spain, and UK)

Global Endometriosis Therapeutics Market Expected to Decrease at a Compound Annual Growth Rate of 0.19% During 2012–2017

GlobalData estimates that the global endometriosis therapeutics market in the 6MM was valued at $1.88 billion in 2012. The market was largely dominated by the US, with sales of $1.1 billion. Combined sales in the 5EU were estimated at $137.6m. By 2017, GlobalData forecasts that global sales of endometriosis therapeutics will decrease slowly to $1.66 billion at a Compound Annual Growth Rate (CAGR) of 0.19%.

By the end of the forecast period in 2017, GlobalData foresees that market growth will remain driven by the US, with marginal changes in the 5EU share by 2017. The patent expiry of Lupron (leuprolide acetate) in 2014 is expected to have a negative effect on this market. However, since it is a sterile injectable drug, GlobalData has tempered the potential effect of this event, as manufacturers may face barriers when attempting to create generic equivalents.

The figure below illustrates the global sales for endometriosis therapeutics by region during the forecast period.

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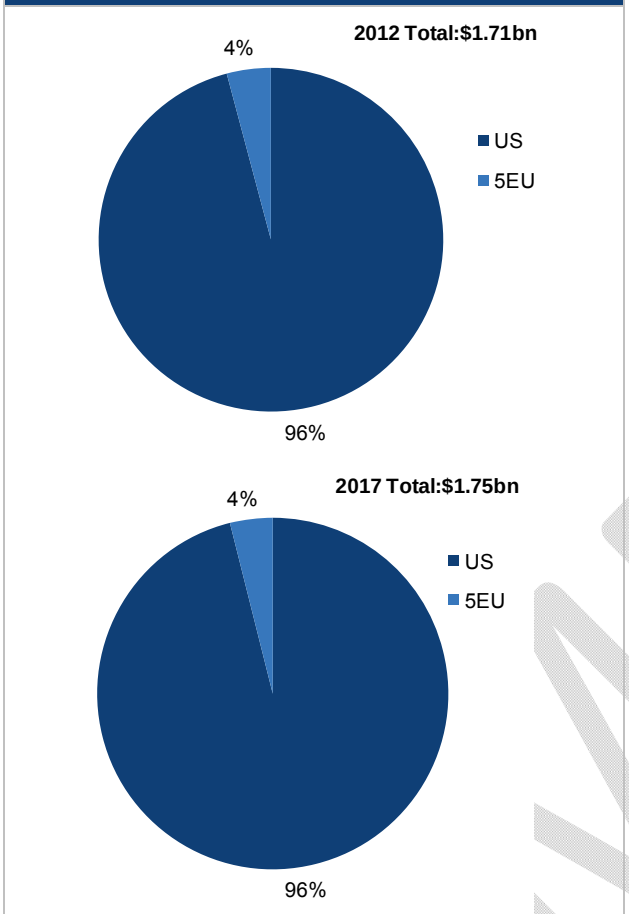
Global Sales for Endometriosis Therapeutics by Region, 2012–2017



Source: GlobalData

Nonetheless, this waning market will regain momentum upon the expected launch of elagolix, a first-in-class oral gonadotropin-releasing hormone (GnRH) antagonist, in the US and 5EU in 2016. Since price is a primary attribute driving therapy choice in this market, new entrants such as elagolix will have little potential to steal share from low-cost therapies such as OCs, NSAIDs, and progestins.

Endometriosis Market Plagued by High Unmet Need

Patients with endometriosis have significant unmet needs due to the lack of approved treatment options that have both continuous efficacy and a favorable long-term safety profiles. Laparoscopic surgery, either alone or in combination with hormone therapy (HT), is typically the first treatment choice for physicians. However, the methods of treating the condition, have been largely haphazard. As a result, women often undergo numerous rounds of surgery and try several medical approaches before finding relief. Even after finding a suitable solution, patients can expect a high rate of recurrence. The current approved treatment options for endometriosis include GnRH agonists, progestins, and androgens, each of which has its own safety and efficacy limitations. Although the use of GnRH agonists has increased in the past decade, the duration of therapy is typically limited to six months due to hypoestrogenic side effects, such as hot flashes, and significant bone mineral density (BMD) loss. Moreover, these drugs come with hefty price tags, which further stifles their appeal for long-term use. NSAIDs and COCs are commonly prescribed off label for confirmed and suspected cases of endometriosis, although their efficacy in this indication has not been validated via randomized clinical trials. Because of the intrinsic limitations of the currently available therapies, innovative drugs with novel mechanisms of action are required in order to address the unmet needs of endometriosis patients.

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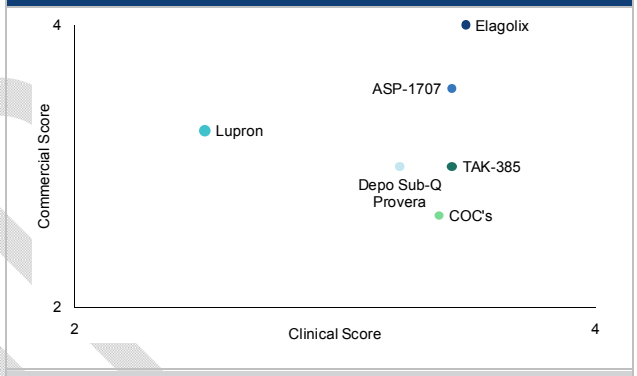
GnRH Antagonists will Replace GnRH Agonists, but Their High Price Will Limit Further Adoption

GnRH antagonists dominate the late-stage pipeline for endometriosis therapeutics, with three agents being in Phase II or Phase III (Abott's elagolix, Takeda's relugolix, and Astellas' ASP-1707). Elagolix, which is in Phase III, promises to be the first oral GnRH antagonist approved for endometriosis. This class of therapies has several key advantages over the currently marketed GnRH agonists. In terms of safety and tolerability, elagolix avoids the detrimental hypoestrogenic side effects seen with GnRH agonists such as Lupron and Zoladex (goserelin acetate). According to key opinion leaders (KOLs) interviewed by GlobalData, an oral formulation will be a welcome addition to the field because it provides doctors with increased control over dosing and allows for the immediate cessation of therapy, if necessary. Therefore, GlobalData believes that GnRH antagonists will rapidly replace the GnRH agonist market segment. Based on their improved efficacy and safety profile, GnRH antagonists like elagolix are likely to be priced at a premium over GnRH agonists such as Lupron. Due to the low cost of progestins, COC's, and NSAIDs, GlobalData believes that the GnRH antagonists are unlikely to take substantial market share away from these drugs. Like GnRH agonists, GnRH antagonists can only be administered for a short period of time, which will restrict their use to late-line therapy and sicker patients. Until more long-term safety data are gathered, and there is evidence that GnRH agonists can be used safely for a longer treatment duration, GlobalData believes that GnRH antagonists will only serve as follow-up drugs to GnRH agonists.

The figure below provides a competitive assessment of the marketed and late-stage pipeline agents in endometriosis therapeutics during the forecast period.

Competitive Assessment of Marketed and Late-Stage Pipeline Agents in Endometriosis Therapeutics, 2012–2017



Source: GlobalData

Opportunity Remains High for Innovative Therapies

Since none of the late-stage drug candidates are meant to address the high unmet need in the endometriosis therapeutics market, the management of the disease is not likely to evolve during the forecast period, and opportunities in the market will remain particularly high. Whether it is for safer drugs or drugs that demonstrate efficacy in mild or severe patients through robust clinical trials, the market is crying for new therapies. Ultimately, since all of the marketed, off-label, and pipeline drugs have little impact in curbing the disease progression, a high rate of recurrence is

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expected upon cessation of therapy. Therefore, large opportunities will remain for safe, efficacious therapies that target the root cause of the condition. Non-hormonal strategies, in particular, are promising, including immune modulators, peroxisome proliferator-activated receptor (PPAR) agonists, tumor necrosis factor-alpha (TNF-alpha) inhibitors, and antiangiogenic agents. In conclusion, a much better understanding of the underlying pathology of this condition will be required in order for a novel therapy to achieve considerable success in the endometriosis market.

What Do Physicians Think?

The consensus among the KOLs interviewed for this report is that endometriosis patients have significant unmet needs due to the lack of safe, efficacious, long-term therapies. Furthermore, significant gaps in the current understanding of the underlying disease pathology were flagged as a hurdle plaguing endometriosis therapy development. Although the KOLs are optimistic about the potential approval of first-in-class therapy, elagolix, they still foresee that unmet needs will persist. One common concern about GnRH antagonist therapy is that it continues to approach the treatment of endometriosis via hormonal pathways. A key limitation is that these drugs do not target the underlying cause of the disease, which means that recurrence is expected to occur once a woman stops therapy. Since endometriosis starts as early as adolescence and can be expected to persist until menopause, any drug that only addresses the symptoms of endometriosis will translate into decades of disease management, rather than resolution of the condition.

One key weakness of the hormonal regimens used to treat endometriosis is that they prevent conception. Given the fact that the majority of women who suffer from endometriosis are of childbearing age, there is a considerable unmet need for a novel therapy that allows for continuation of the normal menstrual cycle and provides for the possibility of pregnancy during treatment. Given the estrogen-dependent nature of endometriosis, the current therapies target the condition by disrupting hormonal pathways which play a key role in fertility. Although some novel therapeutic classes that are under development have shown promising efficacy data, many of these approaches have side effects that would contraindicate their use in women looking to conceive.

"I am sure that GnRH antagonists will be effective. The problem is that women will have recurrences [of endometriosis] once they will discontinue the drug."

EU KOL, October 2013

"Approaching the disease from an inflammatory standpoint would be an innovative approach that I would be interested in seeing."

EU KOL, October 2013

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"We don't know very much about the real mechanism underlying the generation of pain in endometriosis."

US KOL, October 2013

"I believe GnRH antagonists will be yet another class [of drugs] that would be useful in the management of endometriosis."

US KOL, October 2013

"The oral formulation of GnRH antagonists will certainly provide advantages over the injectable GnRH agonists."

US KOL, October 2013

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2 Introduction

2.1 Catalyst

The endometriosis therapeutics market has been in need of innovative therapies for quite a while. Competition in this market has historically been weak due to the lack of approved products. Hormonal therapies have dominated this market, yet the currently approved drugs leave much to be desired in terms of their risk-benefit profiles and long-term efficacy. The endometriosis therapeutics market is expected to experience a flurry of changes over the next five years. Although the market-leading gonadotropin-releasing hormone (GnRH) agonist, Lupron (leuprolide acetate), will lose patent protection in 2014, this change will be offset by the launch of AbbVie and Neurocrine's first-in-class oral GnRH antagonist, elagolix. The entry of elagolix will provide a much-needed jolt to this market. In fact, this product will be the first major innovation in this indication in many years. Being orally active is a major benefit of elagolix, which will potentially offer several advantages over the incumbent injectable GnRH agonists. The GnRH antagonist mechanism of action allows for the rapid onset of estrogen suppression, without the hormonal flare effect seen with the GnRH agonists. Furthermore, the deleterious BMD loss seen with the injectable GnRH agonists is not seen with the GnRH antagonists. Ultimately, elagolix's oral route of administration will be a welcome addition to the therapeutic paradigm that will give doctors more control over dosing and will allow for the titration of circulating estrogen levels. By allowing for modulation of the level of ovarian suppression, elagolix will be a customizable solution, with increased safety over the currently approved drugs. Elagolix's major commercial attribute will be its potential to tap into a larger patient pool than drugs such as the GnRH agonists, Lupron and Zoladex (gosarelin acetate).

2.2 Related Reports

- GlobalData (2013). EpiCast Report: Endometriosis – Epidemiology Forecast to 2022, PHARMAEPIA35167.

Appendix

9.6.3 Global Director of Epidemiology and Health Policy

Franka des Vignes, PhD, currently serves as the Global Director of Epidemiology and Health Policy at GlobalData in New York City, where her primary responsibilities include managing the production and quality of the epidemiology reports and forecast models, improving the epidemiology database, liaising with clients to identify their satisfaction with the existing epidemiology offerings, prioritizing critical unmet needs, and supporting GlobalData teams with consulting opportunities. Prior to joining GlobalData, Franka worked for several years in the public sector to implement and manage several large projects leading to successful disease surveillance programs in the United States. Her experience includes analyzing epidemiological trends, assessing clinical trials, and performing pharmaceutical market forecasting in the private sector. In the nonprofit sector, she served as the Deputy Director of a Washington DC-based organization focused on health policy regarding HIV/AIDS. In the international arena, she has advised national Ministries of Health and has worked for international health organizations such as CAREC/PAHO/WHO to provide technical assistance to governments with health systems' strengthening, patient population databases, and the assessment of surveillance systems in more than 20 countries in the Caribbean and Latin America. Franka holds a Master of Science in Microbiology and a PhD in Epidemiology and Public Health from Yale University.

9.6.4 Global Head of Healthcare

Bonnie Bain, PhD, is Global Head of Healthcare for GlobalData in Boston, managing the Medical and Pharmaceutical arms of the business. Prior to this role, she was Vice President and Global Research & Analysis Director for Informa, where she oversaw the global strategy and operations for Datamonitor Healthcare's syndicated business. Bonnie has over 15 years of experience in the healthcare sector and a proven track record of developing innovative solutions on both the client and vendor sides of the business. Prior to joining Informa, she was Director of Product Development at Wood Mackenzie, where she oversaw the development and management of two product lines. Bonnie also worked for several years at Decision Resources as an Analyst and Project Manager. On the client side of the industry, she worked for several years as a Senior Manager in Marketing Strategy and Analytics at Boston Scientific, where her work contributed to the successful commercialization of the first-ever Access and Visualization Platform at the company. She has a PhD in Biochemistry and Molecular Biology from Purdue University, and was a postdoctoral fellow in molecular pharmacology at the University of Miami School of Medicine.

Appendix

9.7 About GlobalData

GlobalData is a leading global provider of business intelligence in the healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports, and forecasts. Our analysis is supported by a 24/7 client support and analyst team.

GlobalData has offices in New York, Boston, London, India, and Singapore.

9.8 Disclaimer