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CURRENT AND FUTURE MARKET DYNAMICS OVERVIEW

Using a patient-based forecasting methodology, Datamonitor Healthcare estimates that sales of drugs for depression totaled $7.1bn across the US, Japan, and five major EU markets (France, Germany, Italy, Spain, and the UK) in 2015. After contracting to $6.2bn in 2017, the market is forecast to return to growth and reach $9.4bn annually by 2024. This will be driven primarily by the uptake of several pipeline drugs from new therapeutic classes, including the N-methyl-D-aspartate (NMDA) receptor-targeting products esketamine (Johnson & Johnson) and rapastinel (Allergan), as well as the opioid-based ALKS 5461 ([buprenorphine + samidorphan]; Alkermes). To a lesser extent, recently launched products such as Trintellix (vortioxetine; Lundbeck/Takeda) and Rexulti (brexpiprazole; Otsuka/Lundbeck) will continue to grow their patient shares, although continued generic erosion among traditional drug classes will limit their commercial potential. Over the entire 2015–24 period, the depression market is expected to expand at a compound annual growth rate of 3.1%.

Figure 1: Depression sales across the US, Japan, and five major EU markets, by country, 2015–24
SSRI AND SNRI ANTIDEPRESSANTS WILL REMAIN THE MAINSTAY OF TREATMENT

The two traditional antidepressant classes – the selective serotonin reuptake inhibitor (SSRI) and serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants – will form the backbone of therapy for most depression patients. SSRIs will also have the highest cumulative sales over the forecast period of any drug class. Both the SSRI and SNRI class are very well established in the treatment paradigm and are also commercially mature, with generic equivalents of the leading molecules in each class widely available. While the market opportunity for patent-protected brands in these classes is now smaller due to this competition, increasing drug prices in the US will allow for the majority of the value to be retained. Products set to capitalize on this include Trintellix, Viloryd (vilazodone; Allergan), and Fetzima (levomilnacipran; Allergan).

Conversely, the atypical antipsychotic class is less mature and will decline in the short term as Abilify sales are further eroded by generics. The ongoing uptake of Rexulti will help to offset further loss in value among the class when AstraZeneca loses protection for Seroquel XR (quetiapine) in the US and certain EU markets. However, no further advancement in the class is expected, as clinical trial programs for Vraylar (cariprazine; Allergan/Gedeon Richter/Mitsubishi Tanabe) and Latuda (lurasidone; Sumitomo Dainippon/Sunovion) have now stalled.

Figure 2: New class sales in the context of the wider depression market across the US, Japan, and five major EU markets, 2015–24
PHARMACOLOGICAL VERSUS NON-PHARMACOLOGICAL

Pharmacological treatment becomes a standard of care with disease severity

An abundance of different treatment options exist for depression, and physicians treating a patient must decide on the most appropriate course of action. Initially, they must make a choice between different treatment modalities and whether pharmacological treatment, non-pharmacological methods, a combination of the two, or no treatment at all may be a best first step. There are pros and cons associated with each modality and the selection can be pivotal in determining the patient’s ultimate outcome. This decision is guided by the severity of the patient’s symptoms, the availability of both pharmacological and non-pharmacological therapies, patient preference and contraindications, instructive guidelines, and physician experience.

Examples of non-pharmacological approaches for depression include psychotherapy (ie cognitive behavioral therapy and interpersonal therapy), exercise, and neurostimulatory interventions for severe, treatment-resistant depression.

Pharmacological treatment is the mainstay of treatment for depression in the US, Japan, and five major EU markets (France, Germany, Italy, Spain, and the UK). The majority of patients, regardless of whether they are suffering from dysthymia or major depressive disorder (MDD), receive active drug treatment for their depression symptoms. On average, physicians surveyed in Datamonitor Healthcare’s primary research revealed that 66.7% of dysthymia patients and 85.4% of MDD patients receive drug therapy, either as the sole therapy or in combination with a non-drug intervention. The drug treatment rate of dysthymia is notably lower than for MDD as the symptoms are less severe and more tolerable for patients, especially in light of possible unwanted side effects from pharmacotherapy.

This trend is similar across the US and five major EU markets. However, in Japan, patients are less likely to receive a non-drug therapy. In fact, 87.4% of dysthymia patients in Japan receive pharmacological treatment, which is almost as high as the 92.0% pharmacological treatment rate of MDD patients. Psychotherapy, a common treatment modality for dysthymia, is a less attractive option among Japanese patients and their physicians. For one, it is not economically supported by the Japanese national health insurance system. In addition, psychotherapy is an uncommon concept to Japanese culture (The Wall Street Journal, 2002).
**TOTAL PREVALENT CASES OF DYSTHYMIA**

- Datamonitor Healthcare estimates that in 2017, there were 7.0 million total prevalent cases of dysthymia in the US, Japan, and five major EU markets.

- By 2037, Datamonitor Healthcare forecasts that the number of total prevalent cases of dysthymia in the US, Japan, and five major EU markets will increase to 7.3 million. This trend is driven by demographic changes only, as Datamonitor Healthcare held the prevalence proportions constant throughout the forecast period.
**Figure 50**: Datamonitor Healthcare’s drug assessment summary for Lexapro in depression

Source: Datamonitor Healthcare
EXTENSIVE DEVELOPMENT PROGRAM ESTABLISHES TRINTELLIX’S EFFICACY

The efficacy and safety of Trintellix was evaluated in an extensive Phase III development program. Although early Phase III low-dose trials did not provide strong evidence for Trintellix’s efficacy, Lundbeck and Takeda overcame any early concerns with the drug’s lack of efficacy, in the end providing strong evidence for its efficacy in its late-stage development program. The FDA has approved Trintellix based on six short-term Phase III studies and one long-term maintenance study. In each of the six short-term studies at least one dose of Trintellix demonstrated statistically significant superiority to placebo in the improvement of depressive symptoms. The long-term maintenance study also revealed Trintellix’s statistical superiority to placebo in time to recurrence of depressive symptoms (Trintellix, 2016).

The efficacy of Trintellix was demonstrated across a range of doses (from 5mg to 20mg), and the recommended starting dose is 10mg. Trintellix is available in 5mg, 10mg, 15mg, and 20mg tablets, providing flexibility to prescribers and patients in order to achieve the right balance between efficacy and tolerability.

Importantly, one of the six pivotal studies included elderly patients, and positive data from a long-term maintenance (relapse prevention) study included in the product label allow Lundbeck and Takeda to make broad claims with regards to Trintellix’s efficacy (Trintellix, 2016).

Find out more about the full report

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**Figure 63:** Datamonitor Healthcare’s drug assessment summary for Trintellix in depression

![Datamonitor Healthcare’s drug assessment summary for Trintellix in depression](source)

<table>
<thead>
<tr>
<th>Weighting</th>
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<tr>
<td>Clinical development stage</td>
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</tbody>
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| **Commercial attractiveness** |
| Molecule novelty | ![novelty](image) |
| Size of target population | ![population](image) |
| Disease specific experience | ![experience](image) |
| Commercial resources | ![resources](image) |
| Price | ![price](image) |
| Drug manufacturing cost | ![cost](image) |
| Generic competition risk | ![risk](image) |

*Represents comparator drug scores.

Source: Datamonitor Healthcare