Thomson Reuters Forecast

# Market Insight

## DRUGS TO WATCH IN 2014

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### WHERE THE 2013 DRUGS-TO-WATCH ARE NOW

In January 2013, Thomson Reuters Cortellis for Competitive Intelligence highlighted five drugs to watch that were predicted to achieve significant regulatory milestones that year and make sales of over $1 billion within five years. All five met their main anticipated milestones, although only four are now expected to reach blockbuster status.

January 2013 saw the US launch of Amarin's Vascepa (icosapent ethyl ester) for severe hypertriglyceridemia. This was followed in February 2013 by the US approval of Celgene's relapsed/refractory multiple myeloma drug Pomalyst (pomalidomide); US launch, plus European approval and launch, followed later that year. February 2013 also saw the US approval and launch of Roche's Kadcyla (trastuzumab emtansine, previously referred to as T-DM1) for the second-line treatment of HER2-positive metastatic breast cancer; Japanese and European approvals were also obtained that year. In March 2013, Celgene's apremilast was filed for US approval for psoriatic arthritis, and a PDUFA date of March 21, 2014, was set. In May 2013, GlaxoSmithKline (GSK) and Theravance's Relovair (fluticasone furoate plus vilanterol trifenatate) gained US approval for COPD; US launch, European approval for asthma as well as COPD, and Japanese approval and launch for asthma (although a COPD filing was withdrawn) followed a few months later.

At this time last year, Consensus sales forecasts for Vascepa were $2.070 billion in 2016, rising to $2.963 billion in 2017. However, in October 2013, an FDA panel recommended against approval of the February 2013 sNDA to broaden the indication to include mixed dyslipidemia. By the end of 2013, the FDA had rescinded the SPA for the ANCHOR mixed dyslipidemia trial, which Amarin appealed. A new PDUFA date has not been set. Consensus sales forecasts for the drug now only reach $574.6 million by 2019. In contrast, 2019 sales for Pomalyst, Kadcyla, apremilast and Relovair are forecast to be $1.802 billion, $4.102 billion, $1.212 billion and $2.747 billion, respectively.

### WHAT TO WATCH IN 2014

In last year's report, Thomson Reuters predicted that 2013 would be an interesting and challenging year for the pharmaceutical industry, and questioned whether the five drugs discussed above would demonstrate the enduring power of the blockbuster model of R&D, or whether they would be some of the few remaining such agents in a dwindling supply. The Consensus sales forecasts for the drugs expected to enter the market in 2014 tend to suggest that the latter scenario is playing out, with the vast majority of these drugs predicted to make sales of less than $1 billion by 2019. However, Gilead Sciences' Sovaldi (sofosbuvir), GSK/Theravance's Anoro Ellipta (umeclidinium plus vilanterol) and Gilead's idelalisib are bucking this trend, with 2019 Consensus sales forecasts of $7.518 billion, $3.081 billion and $1.100 billion, respectively.

### SOVALDI

Gilead's oral NS5B polymerase inhibitor Sovaldi was approved by the FDA in December 2013 for treating chronic hepatitis C virus (HCV) infection as a component of a combination antiviral regimen. Approval was based on data from the NEUTRINO, FISSION, POSITRON and FUSION phase III trials, in which Sovaldi was superior to historical controls or placebo, or non-inferior to current therapies, with SVR12 rates of 50 to 90%. The drug will be priced at $7000 per week, with a 12-week course costing $84,000. Sovaldi is also is awaiting approval in Europe, where it has been recommended for approval. Consensus sales of $2.403 billion are forecast for 2014, rising to peak sales of $9.121 billion in 2017.

Gilead is also developing Sovaldi as part of a fixed-dose combination with its NS5A polymerase inhibitor ledipasvir for genotype 1 HCV. Positive data reported in December 2013 from the phase III ION-1, ION-2 and ION-3 trials, which assessed the combination with and without ribavirin, showed that Sovaldi/ledipasvir had the potential to eliminate the need for ribavirin and also interferon injections. US and European filings are planned for the first half of 2014. Consensus sales of $1.116 billion are forecast for 2014, rising to $6.238 billion by 2016.

### ANORO ELLIPTA

GSK/Theravance's Anoro Ellipta is predicted to outsell its developers' 2013 potential blockbuster Relovair in the COPD field, with Consensus sales of $3.081 billion forecast for 2019, compared with $2.747 billion for Relovair. Relovair comprises a long-acting beta 2 agonist (LABA)

bronchodilator (vilanterol) paired with a glucocorticoid receptor agonist (fluticasone furoate), whereas Anoro Ellipta contains two bronchodilators: vilanterol plus the long-acting muscarinic antagonist (LAMA) umeclidinium. The drug was granted US approval for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema, in December 2013, and is to be launched in the first quarter of this year. The drug is also awaiting European and Japanese approval.

In Anoro Ellipta's pivotal trial program, the agent achieved greater improvements in trough FEV1, 0 to 6 h weighted mean FEV1, transition dyspnea index scores and St George's respiratory questionnaire scores compared with vilanterol or tiotropium monotherapy. The global COPD market is huge, with the disease affecting approximately 64 to 329 million individuals and predicted to be the third leading cause of death by 2030. Anoro Ellipta is well positioned to capture a large share of this market, as treatment guidelines recommend combining long-acting bronchodilators with differing mechanisms of action.

## IDELALISIB

Idelalisib is an oral PI3K p110-delta subunit inhibitor belonging to Gilead that was filed for US approval for indolent non-Hodgkin's lymphoma (iNHL) in September 2013, and for European approval for chronic lymphocytic leukemia (CLL) and iNHL in October 2013; a US filing for CLL is planned. In the phase II DELTA trial for previously treated iNHL refractory to Rituxan (rituximab) and alkylating agents, the overall response rates for follicular lymphoma, small lymphocytic lymphoma (SLL), lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia and marginal zone lymphoma were 65, 61, 80 and 47%, respectively. Phase III trials are underway, with data expected in 2022. Significant efficacy has been demonstrated in a phase III CLL trial, with a progression-free survival rate at 24 weeks of 93% for idelalisib plus Rituxan, compared with 46% for Rituxan alone; the trial was halted early to allow the Rituxan-only recipients to switch to idelalisib treatment. Sales of idelalisib are forecast to exceed $1 billion by 2017, with Consensus sales forecasts of $1.218 billion that year.

Idelalisib will face stiff competition in the CLL market from, among others, Roche and Biogen Idec's Gazyva (obinutuzumab) and Pharmacyclics and Johnson & Johnson's Imbruvica (ibrutinib). Gazyva, a third-generation glycoengineered follow-on to the anti-CD20 mAb Rituxan, was launched in the US for CLL in November 2013, following phase III data that showed that Gazyva plus chlorambucil increased median progression-free survival to 23.0 months compared with 11.1 months for chlorambucil alone. It is currently awaiting European approval for CLL, and is in phase III development for NHL and diffuse large B-cell lymphoma (DLBCL; aggressive NHL). Gazyva Consensus sales of $1.522 billion are forecast for 2019. The Bruton's tyrosine kinase inhibitor Imbruvica was launched onto the US market for mantle cell lymphoma (MCL) in November 2013, and a US filing for CLL and SLL has been assigned a PDUFA date in late February 2014. In October 2013, the drug was filed for European approval for CLL, SLL and MCL. The CLL/SLL filings are supported by phase III data in which overall, complete and partial response rates of 81, 12 and 69%, respectively, were seen. Development is also ongoing for other hematological neoplasms, with filings for Waldenstrom's macroglobulinemia and follicular lymphoma expected between 2013 and 2017, and filings for frontline DLBCL and relapsed or refractory multiple myeloma expected after 2017. Consensus forecasts predict sales of $1.454 billion by 2016, rising to $4.310 billion by 2019.

## BEST OF THE REST

Although Consensus sales forecasts for the majority of drugs predicted to launch in 2014 fall below $1 billion, there are a number of high-sales-potential drugs also worth watching. Eli Lilly hopes to launch its long-acting GLP-1 analog dulaglutide for diabetes and its anti-VEGFR2 mAb Cyramza (ramucirumab) for gastric cancer. The drugs have 2019 sales forecasts of $974.2 million and $904.4 million, respectively, and had both been filed for US and European approval by October last year. MannKind's NDA filing for its inhaled insulin product, Afrezza (formerly Afresa), has been set a PDUFA date of April 15, 2014, potentially enabling a 2014 launch. However, this is the third filing for the drug since the original NDA was submitted in March 2009, after the FDA twice requested further data be provided, and it remains to be seen whether it will be third-time-lucky MannKind. Should the drug reach the market, Consensus forecasts predict sales of $746.2 million in 2019.

## SUMMARY

This year should see some very interesting and novel agents enter the marketplace, including three potential blockbusters - Sovaldi for HCV, Anoro Ellipta for COPD and idelalisib for iNHL and CLL. However, the decline in the number of expected blockbusters in recent years correlates with the anticipated decline of the blockbuster-model of R&D development as such agents become harder to come by. As developing a blockbuster becomes more difficult, the pharmaceutical industry must seek to find replacements for these revenue streams, for example by turning to more personalised therapies. The continued decline in the number of blockbusters, combined with patent expiry for several existing blockbuster agents this year, should make 2014 particularly challenging for the industry.