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Contents

New Therapies To Struggle Against Established Haematology Players

BMI View: *New drugs from smaller biotechs offer distinct advantages over the current therapies, which is their way into the market. However, they are only expected to get a small market share, unless there is the opportunity for a partner. Big pharma have established expertise and will continue to reinforce approved drugs with positive long-term results to fend off competition.*

At the European Hematology Association (EHA) 2017 annual meeting, big pharma's focus was to reinforce data from already approved products. We have previously highlighted a similar theme at ASCO 2017 (*see 'Long-Term Data Key To Maintaining Oncology Dominance', June 13 2017*) and we expect these larger players in the oncology market to make announcements regarding their pipeline later in 2017. In addition, the smaller biotechs have highlighted some positive results from their novel approaches, in an attempt to eventually claim a market share.

Reinforcing Data To Support Growth Of Approved Products

One of the main themes highlighted at the 2017 EHA was the reinforcement of data for already approved products. These big companies need to maintain visibility and any positive data can boost their revenues.

AbbVie presented results from the Phase II study of *Venclyxto* (venetoclax), a first-in-class oral B-cell lymphoma-2 inhibitor. *Venclyxto* monotherapy responses in 158 patients with relapsed/refractory (r/r) chronic lymphocytic leukaemia (CLL) and 17p deletion showed that 77% (95% confidence interval: 69.9, 83.5) achieved an overall response rate (ORR), 18% achieved a complete remission and 53% achieved a partial remission. The drug is jointly commercialised by AbbVie and **Genentech** (**Roche**) in the US and by AbbVie outside of the US.

Also, Roche reported new data from additional analyses of the Phase III GALLIUM study in people with previously untreated follicular lymphoma (FL). The data confirmed that the improvement in progression-free survival with *Gazyva/Gazyvaro* (obinutuzumab)-based treatment over *MabThera/Rituxan* (rituximab)-based treatment was sustained in an updated analysis with a further six months of follow-up, irrespective of chemotherapy regimen. In addition, health-related quality of life as reported by people in the *Gazyva/Gazyvaro* treatment group improved from the baseline assessment, suggesting that lymphoma-related symptoms were reduced by treatment and that this improvement was not diminished by treatment-related side effects. The drug is an engineered monoclonal antibody designed to attach to CD20.

Novartis reported new data from two trials, ENESTfreedom and ENESTop, which demonstrate that approximately half of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia (CML) in the chronic phase, were able to maintain treatment-free remission (TFR) after stopping treatment with *Tasigna* (nilotinib) both in the first-line setting and after switching from *Glivec* (imatinib). *Tasigna* is the first and only TKI to include information on TFR in the EU label. This data provides further evidence of the durability of molecular response following discontinuation of TKI treatment in certain patients with CML.

Bristol-Myers Squibb presented four-year follow-up data from the Phase III ELOQUENT-2 study in which *Empliciti* (elotuzumab) plus lenalidomide/dexamethasone (Ld) continued to demonstrate efficacy in patients with r/r multiple myeloma (MM),

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Highlights

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compared to patients treated with Ld alone. The results presented claim to offer the longest follow-up efficacy and safety data of an immuno-oncology agent. These extended four-year follow-up data demonstrated that adding *Empliciti* to Ld yielded clinically relevant improvements and reductions in the risk of disease progression or death for patients with r/r MM, compared to Ld alone. BMS and AbbVie are co-developing *Empliciti*, an immunostimulatory antibody that targets SLAMF7, with BMS solely responsible for commercial activities.

Takeda To Seek Indication Expansion For Ninlaro

Takeda Pharmaceuticals was one of the few big pharma companies, who published data supporting an approved drug in a new indication. The firm has presented data from two Phase I/II trials evaluating *Ninlaro* (ixazomib) in patients with newly diagnosed MM at the 2017 EHA annual meeting. Both studies evaluated *Ninlaro*+Ld in newly diagnosed patients with MM who did not undergo stem cell transplant, followed by maintenance with single-agent *Ninlaro*. The drug is an oral proteasome inhibitor that is also being studied across the continuum of MM treatment settings as well as systemic light-chain amyloidosis.

These Phase I/II data demonstrate the potential use of *Ninlaro* in combination with Ld in newly diagnosed MM and as a single-agent maintenance therapy, which resulted in patients achieving deepening responses with continual use of the treatment. A total of 86% of patients had Grade=>3 adverse events (AEs) and 52% of patients had serious AEs. Of the two patients who died on study, one was considered to be treatment-related and was due to respiratory syncytial viral pneumonia. There was also one on-study treatment-related death due to cardio respiratory arrest in the single-agent maintenance therapy study. The drug is currently accepted as a second-line treatment option in MM, so further expansion of its indication will help support revenue growth.

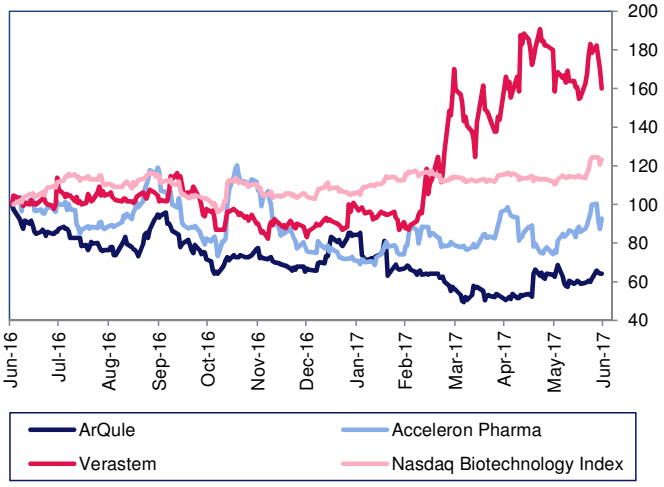
Biotech's Present Positive Data On Novel Therapies

Smaller biotech companies were present at the 2017 EHA annual meeting. These companies have showed varying success with investors' confidence over the last year with **Verastem** outperforming the Nasdaq Biotechnology Index since March 2017. In comparison, **Acceleron Pharma** and **ArQule** have underperformed the comparative index. All of these companies have presented results from new therapies at the 2017 EHA.

Acceleron announced preliminary results from the ongoing Phase II studies of luspatercept in patients with lower-risk myelodysplastic syndromes (MDS). Luspatercept is being developed to treat a range of haematologic diseases, including MDS, beta-thalassemia and myelofibrosis, as part of a global collaboration between Acceleron and **Celgene**. This Phase II update further supports the firms confidence that luspatercept could become a potential first-in-class treatment for lower-risk MDS patients with some patients continuing on study for more than 26 months. The MEDALIST trial, a global Phase III study of luspatercept in patients with lower-risk MDS who require red blood cell transfusions, is fully enrolled and top-line results are expected in mid-2018.

Verastem Outperforms

Select Companies' Equity Performance Normalised Against The Nasdaq Biotechnology Index, 2016-2017



Source: Bloomberg, BMI

Luspatercept is a modified activin receptor type IIB fusion protein that acts as a ligand trap for members in the transforming growth factor-beta superfamily involved in the late stages of erythropoiesis. Luspatercept regulates late-stage erythrocyte precursor cell differentiation and maturation. This mechanism of action is distinct from that of erythropoiesis stimulating agents, which offers it an advantage over competitors.

ArQule published preclinical data for ARQ 531 in diffuse large B-cell lymphoma *in vitro* and *in vivo* tumour models. ARQ 531 is an investigational, orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant BTK. Preclinical data suggests ARQ 531 has the potential for broad clinical utility in a wide range of haematological malignancies and lymphomas. A Phase I trial with ARQ 531 in patients with B-cell malignancies refractory to other therapeutic options, including ibrutinib, is planned to begin by Q317. The only approved BTK inhibitor, ibrutinib,

is irreversible and makes a covalent bond with the C481 residue of the targeted protein. Although ibrutinib has demonstrated excellent responses in patients with elevated B-cell receptor signalling, clinical resistance has been observed, and the BTK C481S mutation is emerging as a predominant mechanism of resistance. This resistance mechanism could offer ARG 531 a potential way into the market.

Verastem presented long-term follow-up data from the DYNAMO study, which met its primary endpoint of ORR (p=0.0001) at the final analysis. DYNAMO is a Phase II study evaluating duvelisib, the company's investigational oral monotherapy, dual inhibitor of PI3K-delta and PI3K-gamma, in patients with indolent non-Hodgkin's lymphoma whose disease is refractory to both rituximab and chemotherapy or radioimmunotherapy. With 18 months of follow-up, the data continues to be consistent with the primary analysis. Of the 83 patients with double-refractory FL enrolled in DYNAMO (median three prior anticancer regimens), 36 responded, which included 1% complete response and 42% partial responses, for an ORR of 43% as determined by an independent review committee. Notably, 83% of evaluable patients with FL treated with duvelisib had a reduction in the size of their target lymph nodes.

AOP Orphan Pharmaceuticals and **PharmaEssentia** announced the latest results from three studies on ropeginterferon alfa-2b for patients with polycythemia vera (PV). Ropeginterferon alfa-2b is a novel, long-acting, mono-pegylated proline interferon expected to be the first interferon approved for PV worldwide. It is currently under EMA review for marketing authorisation in the EU by AOP Orphan, and PharmaEssentia intends to seek its approval by the FDA in the US.

Breast Cancer

Eisai Withdraws Halaven NDA In China

Eisai has temporarily withdrawn NDA for anticancer agent *Halaven* (eribulin mesylate) in China in order to submit additional documentation. No additional clinical trials have been scheduled, and resubmission will take place as soon as the additional documentation is prepared. In July 2016, Eisai submitted a NDA for *Halaven* seeking approval as a treatment for locally advanced or metastatic breast cancer.

CHMP Recommends Faslodex To Treat First-Line MBC

The EMA's CHMP has adopted a positive opinion, recommending the marketing authorisation of **AstraZeneca**'s *Faslodex* (fulvestrant) for the treatment of HR+, locally advanced or metastatic breast cancer (MBC) in postmenopausal women not previously treated with endocrine therapy, or with disease relapse on or after adjuvant anti-oestrogen therapy, or disease progression on anti-oestrogen therapy.

The CHMP recommendation is based on pivotal data from the FALCON (Fulvestrant and AnastrozoLe COmpared in hormonal therapy-Naïve advanced breast cancer), randomised, double-blind, multicentre Phase III trial, where *Faslodex* 500mg demonstrated superiority over *Arimidex* (anastrozole) 1mg in the treatment of locally-advanced or MBC in post-menopausal women who had not received prior hormonal-based medicine for HR+ BC. The FALCON data show that the delay in disease worsening or death (median progression-free survival, PFS) was 2.8 months longer with *Faslodex* than *Arimidex*. The median PFS was 16.6 months in the *Faslodex* arm compared with 13.8 months in the *Arimidex* arm.

Haematological Cancer

Adcetris Meets Primary Endpoint In Phase III Advanced HL Trial

The Phase III ECHELON-1 trial has met its primary endpoint of a statistically significant improvement in modified progression-free survival (PFS) versus the control arm. ECHELON-1 is a randomised, multicentre trial evaluating **Takeda Pharmaceutical/Seattle Genetics**' *Adcetris* (brentuximab vedotin) as part of a frontline combination chemotherapy regimen in 1,334 patients with previously untreated advanced classical Hodgkin's lymphoma (HL).

Patients in ECHELON-1 were randomised to receive either a combination of *Adcetris*+AVD (Adriamycin, vinblastine, dacarbazine) or ABVD (Adriamycin, bleomycin, vinblastine, dacarbazine), a recognised standard-of-care for frontline HL. The results of the ECHELON-1 trial demonstrated that combination treatment with *Adcetris* resulted in a statistically significant improvement in modified PFS versus the control arm as assessed by an Independent Review

Facility (hazard ratio=0.770; p-value=0.035). The two-year modified PFS rate for patients in the *Adcetris* arm was 82.1% compared with 77.2% in the control arm. Interim analysis of overall survival (OS), the key secondary endpoint, also trended in favour of the *Adcetris*+AVD arm. The safety profile of *Adcetris*+AVD in the ECHELON-1 trial was consistent with that known for the single-agent components of the regimen. There was an increased incidence of febrile neutropenia and peripheral neuropathy in the *Adcetris*+AVD arm. The control arm had an increased rate and severity of pulmonary toxicity. Takeda and Seattle Genetics plan to submit these results to regulatory authorities for approval in their respective territories.

Adcetris is an ADC comprising an anti-CD30 monoclonal antibody attached by a protease-cleavable linker to a microtubule disrupting agent, monomethyl auristatin E, utilising Seattle Genetics' proprietary technology. The ADC employs a linker system that is designed to be stable in the bloodstream but to release MMAE upon internalisation into CD30-expressing tumour cells. *Adcetris* is currently not approved as a frontline therapy for HL.

Seattle Genetics and Takeda are jointly developing *Adcetris*. Under the terms of the collaboration agreement, Seattle Genetics has the US and Canadian commercialisation rights and Takeda has rights to commercialise *Adcetris* in the rest of the world. Seattle Genetics and Takeda are funding joint development costs for *Adcetris* on a 50:50 basis, except in Japan where Takeda is solely responsible for development costs.

Novartis' Expertise To Overcome CTL019 Manufacturing Challenges

***BMI View**: Quality of the manufacturing, turn-around time for development and cost of CAR-T therapies will be crucial in the success of these personalised medicines. Kite Pharma's KTE-C19 shorter development time will give it the advantage over Novartis' CTL019 in the short term; however, in the longer term CTL019 will become the market leader due to the company's expansive expertise.*

Manufacturing quality and costs are going to crucial to the market approval of personalised cancer medications. This is due to the extensive process to genetically code each individual patient T-cell, alongside the need for speed in the development. **Novartis** has released data at the European Hematology Association (EHA) annual meeting, June 24-25 to help support its CAR-T therapy in multiple indications.

Kite Pharma and Novartis are currently racing to be first-to-market with their own CAR-T therapies. Novartis is expected to be the first-to-market with the FDA accepting the company's BLA submission and granted it priority review in March 2017. In comparison, Kite completed its rolling BLA submission of KTE-C19 in April 2017 and received priority review in May. Novartis' CTL019 (tisagenlecleucel-T) is currently targeting relapsed and refractory (r/r) paediatric and young adult patients with B-cell acute lymphoblastic leukaemia (ALL) and has a PDUFA date of early October, whereas Kite's KTE-C19 is seeking approval in aggressive B-cell non-Hodgkin's lymphoma (NHL) and has a PDUFA date of November 29. Kite has seen one case of cerebral oedema, reported in April 2017 in the ZUMA-1 trial. These results are being used to seek FDA approval and this severe adverse event could prove problematic in the acceptance of KTE-C19. Novartis is also set to face some challenges before CLT019 sees approval. The FDA has set up an advisory committee to review Novartis' CAR-T therapy on July 12, which will set the tone for future CAR-T approvals.

Novartis Highlights Success Of CLT019

Novartis has reported updated results from the ELIANA trial demonstrating CTL019 remission rates are maintained at six months in r/r paediatric and young adult patients with B-cell ALL. These data from this pivotal trial of CTL019 show that 83% (52 of 63; 95% confidence interval [CI]: 71%-91%) of patients achieved complete remission (CR) or CR with incomplete blood count recovery within three months of infusion. No minimal residual disease was detected among responding patients. Durability is an important measure for children and young adults with r/r B-cell ALL.

Forty-seven percent of patients in ELIANA experienced Grade 3 or 4 cytokine release syndrome (CRS). There were no deaths due to refractory CRS and no incidents of cerebral oedema were reported. Fifteen percent of patients experienced Grade 3 neurologic events, with no Grade 4 events seen. ELIANA is the first paediatric global CAR-T cell therapy registration trial, with study enrolment having occurred across 25 centres in the US, Canada, EU, Australia and Japan.

CLT019 Supported By Data Across Many Haematological Cancers

CTL019 was granted priority review from the FDA in March 2017 in the treatment of r/r paediatric and young adult patients with B-cell ALL, and Novartis plans to file with the EMA later in 2017. The FDA also granted breakthrough therapy designation to CTL019 for the treatment of adult patients with r/r diffuse large-b-cell lymphoma (DLBCL),

whose disease has progressed on or after two or more prior therapies. Novartis has highlighted the success of CLT019 in many presentations at the 2017 EHA annual meeting. These include:

- A pooled data analysis from two multicentre trials of CTL019 in paediatric and young adult patients with r/r B-cell ALL aimed to identify any new safety issues with CTL019 as a result of its use in multicentre trials, which included 25 sites across 11 countries. Study authors concluded that there were no new safety issues and that CRS and neurologic events were effectively managed. Prolonged follow-up will be required to determine the long-term safety of B-cell aplasia.
- An oral presentation featured pooled analyses from two multicentre trials of CTL019 in paediatric and young adult patients with r/r B-cell ALL observing response analysis and impact of intrinsic/extrinsic and manufacturing factors on CTL019 expansion and persistence. There was increased expansion of CTL019 with higher tumour burden at enrolment, which correlated with higher CRS grade. There was no relationship between dose and expansion, supporting the wide dose range used. Expansion was not attenuated by tocilizumab or steroids.
- Novartis also presented an encore of results from its global, multicentre Phase II JULIET study, evaluating CTL019 in adults with r/r DLBCL. This planned interim analysis confirms the high response rates and durable CRS observed in the previous single-centre experience in a cohort of highly pretreated patients. Centralised manufacturing was feasible. CTL019 was generally tolerated without instance of treatment-related mortality.

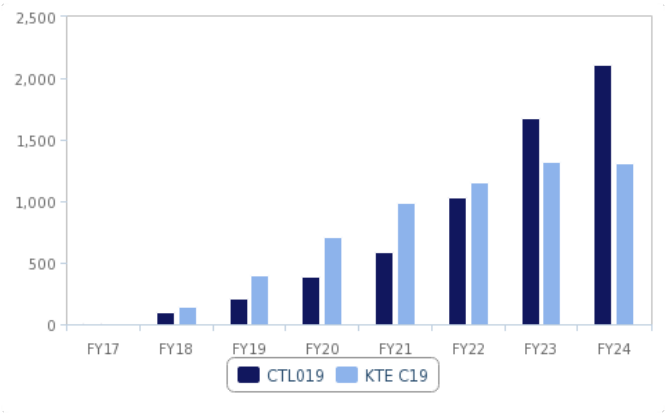
Manufacturing To Remain Crucial To CAR-T Success

Novartis' leukapheresis process using cryopreservation allowed for manufacturing and treatment of patients from around the world. The total manufacturing process includes taking blood from the patient, which is then cryopreserved, shipped to a facility, reprogrammed and manufactured and then shipped back to the patient for infusion. All of these need to be completed in the shortest time possible. Cryopreserved leukapheresis gives physicians the flexibility to schedule apheresis at a time that is in the best interest of their patients. Novartis' commercial manufacturing for CTL019 continues to build on its experience in its facility in Morris Plains, New Jersey, which **Dendreon** sold for USD43mn in 2012. Dendreon was acquired by **Valeant Pharmaceuticals** in 2015.

Novartis officials expect to have a turnaround time of 22 days for its CAR-T treatment, with 10-12 of those days being the cell processing time. The company claims to be looking at processes to speed this up without damaging the effectiveness of the therapy. The continuous improvements in its manufacturing process over the course of its JULIET trial has led to an increase in the manufacturing success rate to 97% for the last 30 patients. This follows earlier issues in which nine of 141 patients had to discontinue treatment due to the ability to manufacture an adequate dose of CAR-T cells.

CLT019 To Become The Leader

Estimated Product Revenues (USDmn)



Source: Bloomberg, BMI

Kite will be producing its rival CAR-T therapy next to Los Angeles airport to expedite receipt and shipment from and to patients across the US and Europe. The firm is anticipating that it can turn around its CAR-T therapy in 14 days. The shorter development time will help Kite to undermine Novartis in the short term, even though CTL019 is expected to be first-to-market. Novartis' established market presence, sales channels and commercial relationships will help CTL019 to become the future market leader.

Besponsa Approval Will Have Limited Impact On Pfizer's Oncology Revenues

BMI View: *The EU approval of Besponsa validates Pfizer resurrecting this once failing compound. It is targeting a haematological cancer that is currently underserved, but the product will not be a growth driver for the company due to the limited target population. Pfizer's oncology portfolio will rest on the performance of Ibrance and the company will need to add to its pipeline to secure sustained growth.*

Pfizer has re-entered the antibody-drug conjugate (ADC) market with the EC approval of *Besponsa* (inotuzumab ozogamicin) as monotherapy for the treatment of adults with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL). This indication includes treatment of adults with Philadelphia chromosome positive (Ph+) as well as Philadelphia chromosome negative (Ph-) relapsed or refractory B-cell precursor ALL. Adults

with Ph+ relapsed or refractory CD22-positive B-cell precursor ALL should have failed treatment with at least one tyrosine kinase inhibitor (TKI). With this approval, *Besponsa* becomes the first and only ADC available for patients with this type of leukaemia in the EU.

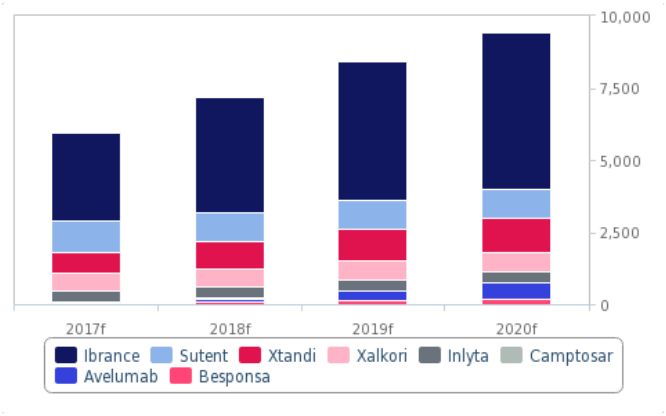
US Approval Not Far Behind

In the US, *Besponsa* is on track for approval in August 2017, or before as the product has priority review and breakthrough designation. As the drug is for a cancer with limited treatment options it is likely that the FDA will expedite the review as it has done with previous cancer drugs with a similar outlook.

Despite aiming for a relatively untapped market, *Besponsa*'s growth will not be rapid. It is expected to reach USD232mn in annual revenues by 2020, far below the rapid growth of the company's strongest oncology compound, *Ibrance* (palbociclib), which is set to reach revenues of USD5.4bn by 2020. *Ibrance* is set to support the growth of Pfizer's oncology segment, even outperforming the company's PD-1 inhibitor, avelumab. In order to drive *Besponsa*'s growth, Pfizer will need to explore use of the drug in other haematological cancers in order to capture a wider target market.

Ibrance To Drive Pfizer's Cancer Ambitions Not Besponsa

Pfizer's Oncology Revenue Forecasts (USDmn)



f = forecast. Source: Bloomberg, BMI

Chequered Past With ADCs

Previously, *Besponsa* failed in Phase III development (*see 'Pfizer Cannot Rely Solely On Resurrecting Shelved Oncology Candidates To Drive Growth', April 23 2015*). In May 2013, Pfizer discontinued a Phase III trial evaluating the safety and efficacy of the drug in patients with relapsed or refractory CD22+ aggressive non-Hodgkin's lymphoma (NHL) when it was established that it would not achieve its primary endpoint. The success in ALL will be a start to *Besponsa*'s growth moving forward.

Pfizer's *Mylotarg* (gemtozumab ozogamicin) was the first ADC to make it to market in 2000, but was later withdrawn in 2010 amidst concerns about the product's safety and efficacy. To manage some of the safety concerns, Pfizer has used smaller and more frequent doses and has boosted efficacy, combining the ADC with chemotherapy. By targeting specific adult AML populations, *Mylotarg* has delivered some promising Phase III results; however, the company is now pursuing *Besponsa*, instead of the relaunch of *Mylotarg.*

Furthering its renewed success in ADC development, Pfizer has another ADC in the pipeline, albeit at an early stage. PF-06647020 is an anti-PTK7 ADC that is comprised of a humanised monoclonal antibody directed against PTK7, which is also expressed in many tumour types, linked to an auristatin microtubule inhibitor payload. It is currently in Phase I trials and the expected completion date for the primary outcome measure is July 2019. The company did have another two Phase I ADCs in development, but there were no longer in the latest pipeline released by Pfizer. With only four novel mid- to late-stage compounds in its oncology pipeline, Pfizer will look for deals to expand its future product pool, and the company may turn to further ADCs to fulfil this.

Lung Cancer

New-Generation Companion Diagnostics To Aid Targeted Therapy Market

BMI View: *The approval of one companion diagnostic for multiple drugs marks an evolution in the precision medicine field. It will drive uptake of targeted therapies while reducing the cost burden of multiple biomarker tests. Expanding the panel to include other cancers and biomarkers will ensure rapid uptake of this testing paradigm.*

Precision medicine is evolving and this has been cemented with the FDA's approval of **Thermo Fisher Scientific**'s next-generation sequencing (NGS)-based test that simultaneously screens tumour samples for biomarkers associated with three FDA-approved therapies for non-small cell lung cancer (NSCLC).

The *Oncomine Dx* target test simultaneously evaluates 23 genes clinically associated with NSCLC. Following FDA approval, results from analysis of three of these genes can now be used to identify patients who may be eligible for treatment with one of the following: the combined therapy of **Novartis**' *Tafinlar* (dabrafenib)+*Mekinist* (trametinib), **Pfizer**'s *Xalkori* (crizotinib) or **AstraZeneca**'s *Iressa* (gefitinib). With this test, physicians can now match patients to these therapies in days instead of several weeks, which it often takes when screening samples one biomarker at a time.

Broad Distribution To Ensure Market Penetration

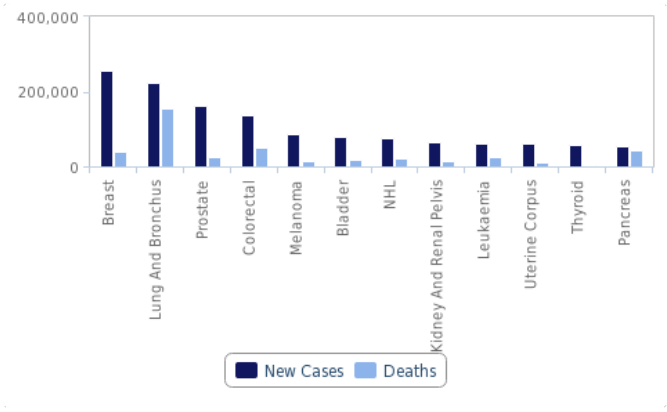
To compete with laboratory developed tests, Thermo Fisher is employing a distribution strategy that will ensure the *Oncomine Dx* test is readily available. **LabCorp**'s Diagnostics and Covance Businesses, **NeoGenomics Laboratories** and **Cancer Genetics**, are among the first laboratories that will offer the *Oncomine Dx* target test as a service to oncologists. All tests will be run on Thermo Fisher's *Ion PGM Dx* system, which received FDA 510(k) clearance in parallel for use on formalin-fixed, paraffin-embedded (FFPE) tissue samples. Laboratory developed tests do not require FDA approval, and the *Oncomine Dx* test will be competing with these.

Expanding Targets Key To Securing Market Share

Lung cancer is a strategic first target. It is one of the most prevalent cancers worldwide with a large number of biomarkers and targeted therapies. Most symptoms present in the late stages of the disease, when the survival rate is only 4%.

Early detection of lung cancer offers the opportunity to reduce mortality. Lung cancer screening is approved for smokers using chest CT scanning. A singular test has the potential to reduce the need for numerous invasive biopsies, and as such, improve health outcomes while reducing the financial impact of diagnosis. This is significant as most lung cancer drugs require confirmatory diagnostics to be used, and a single test to identify the type of lung cancer will be able to direct the next step in diagnostics rather than aim at a wider range.

Lung Cancer Is Significant Target
US Incidence And Death Rate, 2017



Source: NCI's SEER Database, BMI

Thermo Fisher has stated that the newly approved *Oncomine Dx* is just the first iteration of the test. The company will aim to extend the panel to an increased number of biomarkers, which will aid in driving uptake. The process of extending the panel's reach will be quicker than the original approval, and this will aid in promoting acceptance and securing big pharma partners.

Universal Diagnostics Could Change Market Dynamics

As medicine becomes increasingly targeted, diagnostics are heading closer to a 'one size fits all' model. The rise of personalised medicine, especially in the cancer market, has spurred the development of associated genetic tests. These are often for a single genetic marker or biomarker sequence. A number of companion diagnostics that test for a specific mutation can cost as much as whole genome tests. The development of a universal diagnostic that is affordable could replace other genetic tests.

With multiple tests required to determine biomarker status, the adoption of targeted therapies is limited as a result. A drug that does not require a costly companion diagnostic will likely be employed first as a cost saving strategy, especially if a disease is broken down into multiple sub-classifications that require more than one biomarker status test. In addition, multiple tests require multiple samples, especially if the diagnostics are performed by different laboratories, and this can be difficult to obtain. A single test will allow for quicker diagnosis and reduced sample size, which in turn will reduce overall costs.

FDA Approves Tafinlar+Mekinist Combination Therapy For Advanced NSCLC

Novartis has received FDA approval for *Tafinlar* (dabrafenib) in combination with *Mekinist* (trametinib) to treat patients with metastatic non-small cell lung cancer (NSCLC) whose tumours express the BRAF V600E mutation. The FDA granted *Tafinlar+Mekinist* breakthrough therapy designation in July 2015 for the treatment of patients with

advanced or metastatic BRAF V600E mutation-positive NSCLC who received previous treatment with chemotherapy. *Tafinlar+Mekinist* was approved by the EC in March 2017 for the treatment of patients with BRAF V600 mutation-positive advanced NSCLC.

The treatment combination was approved with **Thermo Fisher Scientific**'s *Oncomine Dx* target test to identify a BRAF V600E mutation in eligible patients. This qualitative *in vitro* diagnostic test uses targeted high throughput, parallel-sequencing technology to detect sequence variations in select genes, including BRAF V600E, in DNA and RNA isolated from formalin-fixed, paraffin-embedded tumour tissue samples from patients with NSCLC using the *Ion PGM Dx* system.

EC Approves Label Expansion For Zykadia In Advanced NSCLC

The EC has approved the expanded use of **Novartis**' *Zykadia* (ceritinib) to include the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) whose tumours are ALK-positive. Approval follows a positive opinion granted in May by the CHMP.

The first-line approval of *Zykadia* is based on results from an open-label, randomised, multicentre, global, Phase III trial, ASCEND-4. The study met its primary endpoint, demonstrating a 45% reduction in the risk of disease progression in the *Zykadia* arm, compared with the chemotherapy arm (hazard ratio [HR]=0.55 [95% confidence interval (CI): 0.42, 0.73; one-sided p-value<0.0001]). Patients treated with first-line *Zykadia* had a median progression-free survival of 16.6 months (95% CI: 12.6, 27.2), compared with 8.1 months (95% CI: 5.8, 11.1) for patients treated with standard first-line pemetrexed-platinum chemotherapy with pemetrexed maintenance.

FDA Grants ODD For TPX-0005 To Treat NSCLC

The FDA has granted orphan drug designation (ODD) to **TP Therapeutics'** leading clinical compound TPX-0005 for treatment of non-small cell lung adenocarcinomas harbouring ALK, ROS1, or NTRK oncogenic rearrangements. TPX-0005 is a potent and orally bioavailable small molecule kinase inhibitor for ALK, ROS1 and TRK family.

The clinical benefits of targeting ALK, ROS1, or TRK fusion kinase have been demonstrated with crizotinib, ceritinib, alectinib, and brigatinib, already approved for the treatment of ALK+ non-small cell lung cancer (NSCLC), crizotinib for ROS1+ NSCLC, and larotrectinib and entrectinib in clinical studies for TRK+ cancers. However, the successes of these therapies are overshadowed by the development of acquired resistance. The acquired solvent front mutations including ALK G1202R, ROS1 G2032R, TRKA G595R and TRKC G623R render a common clinical resistance to the current ALK, ROS1, and TRK inhibitors. TPX-0005 is a potent kinase inhibitor against wild type and mutated ALK, ROS1 and TRK family kinases, especially the clinically significant solvent front mutations, gatekeeper mutations, and emerging compound mutations after multiple line treatments.

TPX-0005 will provide new opportunities in the clinic to inhibit the abnormal signalling of ALK, ROS1, or TRK family in solid malignancies, and overcome multiple resistance mechanisms from the refractory patients. TPX-0005 is currently being evaluated in a Phase I/II, open-label, multicentre, first-in-human study of the safety, tolerability, pharmacokinetics and anti-tumour activity in patients with advanced solid tumours harbouring ALK, ROS1, or NTRK1-3 rearrangements (TRIDENT-1).

Gastrointestinal Cancer

eFFECTOR/Pfizer/Merck KGaA To Evaluate eFT508+Avelumab In Advanced CRC

eFFECTOR Therapeutics has entered into a clinical collaboration and supply agreement with **Pfizer** and **Merck KGaA** to evaluate the combination of two immuno-oncology agents in patients with microsatellite stable colorectal cancer (CRC). The companies plan to initiate a Phase II open-label, randomised, non-comparative study to evaluate the safety, tolerability and efficacy of eFFECTOR's investigational small molecule MNK1/2 inhibitor, eFT508, in combination with avelumab in microsatellite stable relapsed or refractory CRC patients.

The study will also include a monotherapy arm investigating eFT508 alone. Patients will be randomised 2:1 between the combination arm and the monotherapy arm. The study is expected to begin in Q317 and will be conducted by eFFECTOR Therapeutics. Pfizer and Merck KGaA, will share the clinical study costs with eFFECTOR. Each party will provide their respective agent for the trial. The collaboration builds upon promising preclinical data providing a scientific

rationale for combining eFT508 with checkpoint inhibitors. In immunocompetent *in vivo* models, eFT508 induced anti-tumour immunity and immune memory as a single agent and, importantly for this collaboration, acted synergistically in combination with checkpoint inhibitors.

Eisai Seeks Japanese Approval For Lenvima In HCC

Eisai has submitted an application for an additional indication of its in-house discovered and developed anticancer agent *Lenvima* (lenvatinib mesylate) for the treatment of hepatocellular carcinoma (HCC) in Japan. The application is based on the results of a multicentre, open-label, randomised, global Phase III trial (Study 304) comparing the efficacy and safety of *Lenvima* versus sorafenib, a standard treatment for advanced HCC, as a first-line treatment for 954 patients with unresectable HCC. Following the application in Japan, Eisai plans to submit regulatory applications for *Lenvima* for the treatment of HCC in the US and Europe during the H117, and in China within FY17.

According to the results of this study, *Lenvima* met the statistical criteria for non-inferiority in the primary endpoint of overall survival (OS) compared with sorafenib. Additionally, *Lenvima* showed highly statistically significant and clinically meaningful improvements in the secondary endpoints of progression free survival, time to progression, and objective response rate, doubling sorafenib's median values and ratios. In this study, the five most common adverse events observed in the *Lenvima* arm were hypertension, diarrhoea, decreased appetite, weight loss and fatigue, which is consistent with the known side-effect profile of *Lenvima*. *Lenvima* is the first agent to meet the statistical criteria for non-inferiority of OS compared with sorafenib since sorafenib was approved for the treatment of HCC 10 years ago.

Lenvima is approved as a treatment for refractory thyroid cancer in over 50 countries, including the US, Japan, and in Europe. Additionally, *Lenvima* in combination with everolimus is approved for the treatment of renal cell carcinoma (RCC) in the US, and in Europe. In Europe, *Lenvima* was launched under the brand name *Kisplyx* for RCC.

Bayer's Stivarga Receives Positive CHMP Opinion For HCC

The EMA's CHMP has adopted positive opinion for recommending **Bayer**'s *Stivarga* (regorafenib) for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with *Nexavar* (sorafenib). The product recently gained approval in the US for second-line treatment of HCC and additional regulatory filings for *Stivarga* in HCC are under review in countries around the world, including China.

The positive opinion is based on data from the international, multicentre, placebo-controlled Phase III RESORCE (REgorafenib after SORafenib in patients with hepatoCEllular carcinoma) trial, which investigated patients with HCC whose disease had progressed during treatment with *Nexavar*. In the trial, *Stivarga* plus best supportive care (BSC) was shown to provide a statistically significant and clinically meaningful improvement in OS versus placebo plus BSC (hazard ratio [HR] 0.63; 95% CI 0.50-0.79; p<0.0001), which translates to a 37% reduction in the risk of death over the trial period. The median OS was 10.6 versus 7.8 months for *Stivarga* and the placebo groups, respectively. Adverse events observed in the trial were generally consistent with the known safety profile of *Stivarga*. The most common treatment-emergent adverse events (Stivarga vs placebo group) were hand-foot skin reaction (53 vs 8%), diarrhoea (41 vs 15%), fatigue (40 vs 32%) and hypertension (31 vs 6%).

FDA Approves Vectibix' sBLA To Treat Advanced MCRC

The FDA has granted sBLA for **Amgen**'s *Vectibix* (panitumumab) for patients with wild-type RAS metastatic colorectal cancer (mCRC) as first-line therapy in combination with FOLFOX and as monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy. *Vectibix* is believed to be the first-and-only fully human monoclonal anti-EGFr antibody approved by the FDA for this patient population. As part of this indication, the FDA approved the first multigene, next-generation sequencing-based test to identify the RAS mutation status of a patient's tumour.

FDA Grants ODD For Propanc Biopharma's PRP Solution To Treat PC

The FDA has granted orphan drug designation (ODD) for **Propanc Biopharma**'s lead product, PRP, a solution for once daily intravenous administration of a combination of two pancreatic proenzymes trypsinogen and chymotrypsinogen, for the treatment of pancreatic cancer (PC). Recent development progress for PRP includes successful completion of a GLP-compliant, 28-day repeat-dose toxicity study with no toxicological findings after administration, indicating a broad safety margin and providing sufficient data to support a safe starting dose for First-In-Human studies. The

company has also commenced development of the GMP-compliant investigational medicinal product manufacture of PRP to support preparation of a planned clinical trial application in the UK. Currently progressing towards first-in-human studies, PRP aims to prevent tumour recurrence and metastasis from solid tumours.

General Developments

OncoArendi Selected OATD-02 For Clinical Development To Treat Cancer

OncoArendi Therapeutics has selected OATD-02 as its clinical development candidate for cancer immunotherapy. Submission of the company's second IND application is expected by Q318. OATD-02 is a highly potent and selective small molecule inhibitor of two arginase isoforms (Arg-1 and Arg-2) in both biochemical and cell-based-assays. OATD-02 is the second arginase inhibitor to enter development.

OATD-02 has been shown to be effective *in vivo* in three different mouse models of cancer (colorectal, lung and melanoma) and demonstrated superior antitumor efficacy in combinations with the PD-L1 checkpoint inhibitor and with gemcitabine; resulting in a controlled tumour growth, and, in some cases in a full regression. Pilot studies also suggested a therapeutic potential of OATD-02 in glioblastoma multiforme. Formal pre-clinical development of OATD-02 will be initiated in July 2017 with GLP toxicology studies expected in Q417 and first in human studies anticipated in Q318. OATD-02, are protected by two pending patents covering two structurally different groups of compounds.

Glenmark Enters Licensing Deal For APC Oncology Compound

Glenmark Pharmaceuticals has entered into a licensing agreement with **APC Therapeutics** for exclusive rights to a small molecule, oncology compound based on antigen presenting cell (APC) biology. The compound has the potential to be used as a monotherapy or in combination with approved therapies to address unmet needs in cancer treatment.

Under the terms of the agreement, Glenmark will license the product from APC Therapeutics, and manage all clinical development including regulatory filings and commercialisation worldwide. APC Therapeutics will receive development milestones and sales royalty payments.

Ewopharma Acquires Rights To Halaven/Targretin/Zonegran In Central Eastern Europe

Ewopharma has acquired the rights to commercialise several of **Eisai**'s products in 11 countries in Central and Eastern Europe (CEE). Ewopharma will commercialise *Halaven* (eribulin mesylate) in nine countries within the EU (Bulgaria, Croatia, Estonia, Hungary, Latvia, Lithuania, Poland, Romania and Slovenia) and in two countries outside of the EU (Bosnia&Herzegovina and Serbia). Ewopharma will also commercialise *Targretin* (bexarotene) in Hungary and Poland as well as *Zonegran* (zonisamide) in Hungary.

Ewopharma will be responsible for all aspects of pricing, reimbursement, marketing and distribution. Eisai will supply product and also provide significant product training and support across the relevant brands.

Servier/Transgene Enter Research Deal On Viral Vectorisation Technology

Servier and **Transgene** have signed a research agreement on the application of viral vectorisation technology for the production of allogenic CAR-T cell therapies. The aim is to obtain more efficient products for patients. The aim of the collaboration between the scientific teams at both Servier and Transgene is to evaluate and select innovative vectorisation methods based on Transgene's viral vector collection, which may be applied to the engineering of CAR-T cell therapies. In addition to the development of simpler, faster and more effective methods, the aim is also to obtain a tighter control of the modified genome areas. Servier and Transgene thus aim to achieve an original allogenic CAR-T preparation method with better transgene integration yields and fewer steps.

Transgene has a large collection of viral vectors and is renowned for its competence in the genome engineering of these vectors. These assets will be used to develop new vectorisation tools that will allow the company to increase the possibility of fine and precise modification of the genome of CART cells, in order to adapt these cells' properties to the tumour environment and improve the therapeutic efficacy. Transgene may receive more than EUR30mn (USD34.2mn) for this contract, with an initial duration of three years. As for Servier, it will be able to use these new vectors to develop its cell immunotherapy portfolio.

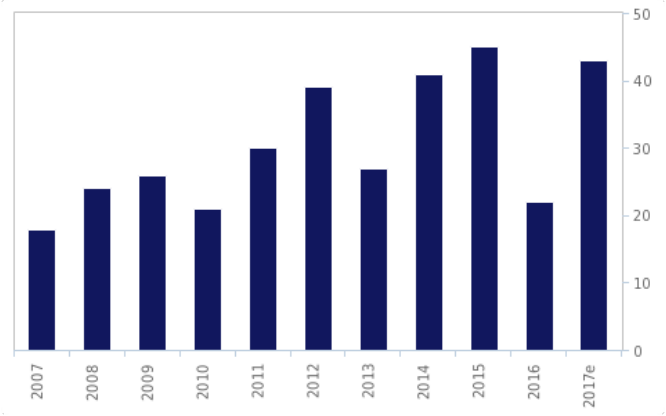
FDA Approvals On Track For Record Year In 2017

BMI View: *2017 will be a record year for new drug approvals. Cancer will lead the approvals, following the trend from previous years, but 2017 will see drugs approved in therapy areas that have not seen new options for quite some time. Highly anticipated drugs with expected high prices will be the standout products of 2017.*

After a slump in the number of NME approvals in 2016, as expected 2017 is set to be a standout year with 23 NME approvals so far plus a sizeable number of products awaiting their FDA fate (*see 'FDA Approvals To Increase In 2017', January 13 2017*). The number already exceeds the 22 approved in 2016, with cancer drugs once again having a significant presence in 2017. A bout of filings at the end of 2016 and early in 2017 is reflected in the high number of total approvals expected in 2017.

Expected Approvals Rebound En Route To Occur

FDA NME/BLA Approvals



e = estimate. Source: FDA, BMI

There are currently 19 NDAs and BLAs with confirmed PDUFA dates in 2017, and a large number of these are likely to gain approval, bringing the total to approximately 43 NMEs approved in 2017 including those with no confirmed PDUFA dates. Notably, **Johnson & Johnson** filed two autoimmune drugs in 2016 and has not released the PDUFA date, but this is likely to be in 2017. The FDA has also managed to approve a number of drugs before their scheduled PDUFA dates; six in total were significantly before their scheduled dates so far in 2017. This could also provide scope for truly innovative drugs filed in H217 to be approved within six months, adding to a record year for drug approvals.

Orphan Drugs And Cancer Therapies Lead Approvals So Far

The approvals so far in 2017 have been dominated by cancer and rare diseases. One drug for a rare disease has caused controversy with high pricing; **BioMarin Pharmaceutical**'s *Brineura* (cerliponase alfa) became the first treatment approved to treat children with neuronal ceroid lipofuscinosis Type 2 (CLN2) disease, a form of Batten disease also known as tripeptidyl peptidase 1 (TPP1) deficiency. It is priced at USD702,00 per year, which reflects the rarity of the disease, but does not include discounts, rebates or patient assistance programmes, which are expected to bring the average price per patient, per year down to USD486,000.

Other notable approvals so far in 2017 include **Valeant Pharmaceutical**'s *Siliq* (brodalumab), a drug for moderate-to-severe plaque psoriasis that both **Amgen** and **AstraZeneca** abandoned due to serious adverse events; *Siliq* poses a potential suicide risk and has a boxed warning. Furthermore, another two PD-1 inhibitors have gained FDA approval in 2017, adding to a crowded market, with **Pfizer**/**Merck KGaA** and AstraZeneca following behind market leaders. **Novartis** has had two cancer drugs approved, and is expecting another approval later in the year, which will aid in rejuvenating its tired oncology portfolio. In addition, **Roche** finally gained approval for *Ocrevus* (ocrelizumab) as the first and only medicine for both relapsing and primary progressive forms of multiple sclerosis (MS).

2017 NME/BLA Approvals So Far

Company	Brandname	INN	Indication
Portola Pharmaceuticals	BEVYXXA	betrixaban	For the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalised for an acute medical illness
Melinta Therapeutics	Baxdela	delafloxacin	To treat patients with acute bacterial skin infections
Sanofi	Kevzara	sarilumab	To treat adult rheumatoid arthritis
Mitsubishi Tanabe Pharma	Radicava	edaravone	To treat patients with amyotrophic lateral sclerosis (ALS)
AstraZeneca	Imfinzi	durvalumab	To treat patients with locally advanced or metastatic urothelial carcinoma
Radius Health	Tymlos	abaloparatide	To treat osteoporosis in postmenopausal women at high risk of fracture or those who have failed other therapies
Novartis	Rydapt	midostaurin	To treat acute myeloid leukaemia
Ariad Pharmaceuticals (Takeda)	Alunbrig	brigatinib	To treat patients with ALK-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib

Company	Brandname	INN	Indication
BioMarin Pharmaceutical	Brineura	cerliponase alfa	To treat a specific form of Batten disease
Neurocrine Biosciences	Ingrezza	valbenazine	To treat adults with tardive dyskinesia
Teva Pharmaceutical Industries	Austedo	deutetrabenazine	For the treatment of chorea associated with Huntington's disease
Roche	Ocrevus	ocrelizumab	To treat patients with relapsing and primary progressive forms of multiple sclerosis
Sanofi	Dupixent	dupilumab	To treat adults with moderate-to-severe eczema (atopic dermatitis)
Tesaro	Zejula	niraparib	For the maintenance treatment for recurrent epithelial ovarian, fallopian tube or primary peritoneal cancers
Shionogi	Symproic	naldemedine	For the treatment of opioid-induced constipation
Merck KGaA	Bavencio	avelumab	To treat metastatic Merkel cell carcinoma
Newron Pharmaceuticals	Xadago	safinamide	To treat Parkinson's disease
Novartis	Kisqali	ribociclib	To treat postmenopausal women with a type of advanced breast cancer
Lexicon Pharmaceuticals	Xermelo	telotristat ethyl	To treat carcinoid syndrome diarrhoea
Valeant Pharmaceuticals	Siliq	brodalumab	To treat adults with moderate-to-severe plaque psoriasis
PTC Therapeutics	Emflaza	deflazacort	To treat patients age five years and older with Duchenne muscular dystrophy (DMD)
Amgen	Parsabiv	etelcalcetide	To treat secondary hyperparathyroidism in adult patients with chronic kidney disease undergoing dialysis
Synergy Pharmaceuticals	Trulance	plecanatide	To treat chronic idiopathic constipation in adult patients

Source: FDA, BMI

H217 Will Be Just As Busy With Approvals

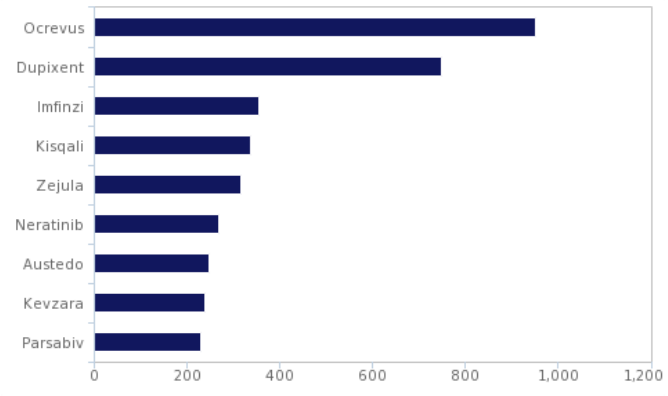
There are at least 19 products awaiting a decision from the FDA in 2017, with a few highly anticipated drugs in the mix. CAR-T therapies will see approval this year. Novartis' CTL019 is scheduled for an advisory committee on July 12, which will set the tone for other CAR-T products awaiting approval, such as **Kite Pharma**'s Kite-019, which has a PDUFA date on November 29. While approval is highly anticipated, questions will surround pricing, which will likely be around the USD500,000 per treatment mark, plus the manufacturing and logistics will be under scrutiny. Off-the-shelf treatments will gain a warmer reception, but these are still in early stages of development.

Celgene is on track to enhance its position in the haematological cancer market with the expected approval of enasidenib by the end of August 2017. The product is an IDH1 mutant inhibitor, for the treatment of patients with relapsed or refractory acute myeloid leukaemia (AML) who have an IDH1 mutation. This is a highly underserved market, and will build upon Celgene's experience with *Vidaza* (azacitidine) in the AML segment of the haematological cancer market.

Osteoporosis has been plagued with trial failures and the treatment landscape primarily consists of older products that are subject to generic competition. However, in 2017, there will be two new treatment options: **Radius Health** has already gained approval for *Tymlos* (abaloparatide) to treat osteoporosis in postmenopausal women at high risk of fracture or those who have failed other therapies, which is a limited target market. Amgen is also aiming to regain market share with romosozumab, which has been filed for the treatment of osteoporosis in postmenopausal women at increased risk of fracture. While the prospects for this drug to be approved in July 2017 were high, data released in May pose a risk to this outlook. An imbalance in positively adjudicated cardiovascular serious adverse events was observed as a new safety signal, which could lead to the drug not gaining approval in 2017.

Oncology Will Be Top Earners Of 2017 Approvals

Top Ten Drugs Approved in 2017 By Forecasted 2018 Revenues (USDmn)



Source: Bloomberg, BMI

Oncology Drugs Will Be Amongst Top Earners

While the biggest earners of drugs approved in 2017 will be a product for MS and one for eczema, cancer drugs will be the primary earners in 2018. *Ocrevus*

and *Dupixent* gained approval earlier in 2017 compared with other drugs in the top 10, which is partly reflected in higher sales, but these also treat areas of unmet need.

CytomX\AbbVie Enter Deal To Advance CX-2029 Development

CytomX Therapeutics has entered into strategic collaboration with **AbbVie** to advanced CX-2029, a probody-drug conjugate (PDC) targeting CD71, into GLP toxicology studies, a key step on the path to file an IND application in 2018. Upon commencement of the study, CytomX will receive an USD15mn milestone payment from AbbVie as part of the 2016 strategic oncology collaboration between the companies.

CytomX and AbbVie are co-developing a PDC against CD71, with CytomX leading pre-clinical and early clinical development. CX-2029 has been designed to target CD71 on tumour cells and spare normal cells by localising the drug candidate's activity primarily to cancer tissue. AbbVie will lead later development and commercialisation with global late-stage development costs shared between the two companies. CytomX received an up-front payment of USD30mn and is eligible to receive up to USD470mn in development, regulatory and commercial milestones, pending the achievement of pre-determined outcomes. AbbVie will lead global commercial activities with CytomX eligible to receive a profit share in the US and tiered double-digit royalties on net product sales outside of the US. CytomX retains an option to co-promote in the US.

Cytovia Reaches Deal On Licensing/Commercialisation Of Ceplene In Latin America

Immune Pharmaceuticals' oncology subsidiary, **Cytovia** has reached substantial agreement on the material terms of a licensing and commercialisation agreement of *Ceplene* (histamine dihydrochloride) in Latin America with **Pint Pharma**. As previously announced on April 20, the company had entered into a letter of intent with Pint, which provided that the parties would use their best efforts to reach agreement regarding the terms of an exclusive licence which would provide Pint the rights to commercialise *Ceplene* throughout Latin America, including Argentina, Brazil, Chile, Colombia and Mexico within 60 days.

The parties have agreed that Pint will be responsible for the registration and commercialisation of *Ceplene* in Latin American countries, and that Pint will base its registration application on the existing EU marketing authorisation for *Ceplene*. In addition, the parties have agreed to enter into a definitive agreement related to Pint's commitment to invest USD4mn into Cytovia at terms similar to other investors in the same financing round and upon satisfaction of certain conditions precedent.

Ceplene is administered in conjunction with low dose interleukin-2 (IL-2), for maintenance of first remission in patients with acute myeloid leukaemia (AML). It has been shown in clinical studies to prevent leukemic relapses in AML patients in first remission and prolong leukaemia-free survival, while maintaining good quality of life during treatment. The drug acts by enhancing the immunostimulatory effect of IL-2 and countering reactive oxygen species-induced dysfunction and apoptosis of T and NK-cells, thereby inducing immune-mediated killing of leukemic cells, providing a strong rationale for this combination therapy. A recent Phase IV study confirmed the safety and efficacy of *Ceplene* in the international study that supported EU approval.

CRT Extends Alliance With Merck To Develop New Cancer Drugs

Cancer Research Technology (CRT) has signed a further deal with **Merck KGaA** to discover new cancer drugs targeting the Hippo pathway. The extension to this alliance follows a successful one-year target validation and drug discovery feasibility partnership between CRT's Discovery Laboratories in London and Cambridge and Merck at Darmstadt in Germany. In conjunction with Cancer Research UK's network of key academic scientists, based at the Francis Crick Institute in London, the alliance has developed a better understanding of the role of the Hippo pathway in cancer, and how best to drug key targets.

In healthy cells the Hippo pathway regulates cell size, controlling the growth of tissues during development and regeneration. But, abnormal activation of proteins controlled by the Hippo pathway has been linked to the development of a range of cancers, making it an attractive area for the discovery of novel therapies. The partnership has now moved into full drug discovery with the aim of eventually identifying molecules to take into preclinical studies and clinical trials. CRT will receive royalties and milestone payments from the deal to be invested into Cancer Research UK's research.

Corporate Activity

Sanpower Completes Takeover Of Dendreon From Valeant

Sanpower has completed its 100% acquisition of **Dendreon** from **Valeant Pharmaceuticals International** for USD819.9mn in cash. Dendreon's core product, *Provenge* (sipuleucel-T), is believed to be the first and only FDA-approved cellular immunotherapy for prostate cancer. *Provenge*'s efficacy and safety have been fully confirmed. It is reimbursed by the vast majority of insures, including Medicare contractors and commercial plans.

Sanpower intends to maintain the continuity of Dendreon's US team, and facilitate the company's continued steady growth through a number of approaches. In particular, Sanpower plans to promote Provenge's penetration outside of the US, starting with China and Southeast Asia. The company's extensive resources in Asia will enable Dendreon to expand its geographic coverage, explore additional clinical programmes and enrich its transaction pipeline with a view to maximise the company's commercial and clinical potential.

IGEM Completes Initial Closing Of Series A Financing

IGEM Therapeutics has closed a GBP2mn (USD2.6mn) series A investment from **Epidarex Capital**. IGEM is now seeking further investment to complete the round. In addition, IGEM has announced the appointment of new CEO. The funding will enable IGEM to continue to invest in pipeline development as it builds its portfolio of IgE antibody candidates, including those that target folate receptor alpha, HER2, EGFr and PD-L1, and will support the further development of IgE antibody platform technology based on protein and glyco-engineering. IGEM believes that potent immune responses arising from IgE are suited to the destruction of solid tumours which also reside in tissue.

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