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Big Pharma Defuses Drug Pricing Landmines On Capitol Hill

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Drug industry leaders faced off with US legislators at a Senate Finance Committee hearing on drug prices Feb. 26, but the tone was more collaborative than confrontational. Industry has reason to be cautiously optimistic after seven of its big pharma leaders got through more than three hours of testimony on drug pricing with relative ease.

Nonetheless, there does appear to be bipartisan support for legislative changes to address the high cost of prescription drugs. Republican senators on the committee delivered some of the more targeted and pointed questions on issues ranging from patent abuses to biosimilar disincentives and even the proposal to link US drug prices to an international pricing index. That could leave industry with a sense of unease, despite having cleared the hearing.

As Chairman Chuck Grassley (R-Iowa) told reporters after the hearing closed, "I'm prepared to legislate, but if you ask me what I plan to legislate, I don't have an answer for that yet." When asked if he thought the big pharma CEOs simply pointed the finger instead of accepting blame, he said, "Not as much as I thought they would." And he added, "We may find out there is a legitimacy to pointing the finger to somebody else down the line."

Click https://bit.ly/2Vzzv5V for our question-by-question infographic which shows how Rx executives exhibited enough finesse to avoid any embarrassing sound bites at the Senate Finance Committee hearing on drug pricing.

The hearing got played up as a big showdown for industry on Capitol Hill in the days leading up to it. Although drug leaders have been called to testify to Congress on a range of issues over the years from drug pricing to drug safety, big pharma's top CEOs have done their best to duck any high-profile appearances in front of Congress in the last 15 years. *(Also see "Senate Drug Pricing Hearing Looms As Unparalleled Event For Pharma" - Pink Sheet, 22 Feb, 2019.)*

Now they might be feeling as though the bark was worse than the bite. Though there were some tense moments and uncomfortable comments about multi-million-dollar CEO salaries, the seven leaders managed to avoid any standout embarrassing confrontations.

Together, they presented a solid collective message: industry wants to work with Congress to lower drug prices, but pharma is just one part of a bigger system that requires cooperation from other partners as well as legislative action.

The seven leaders that testified were **Pfizer Inc.** CEO Albert Bourla, **AstraZeneca PLC** CEO Pascal Soriot, **Sanofi** CEO Olivier Brandicourt, **Johnson & Johnson** Exec VP Worldwide Pharmaceuticals Chair Jennifer Taubert, **Bristol-Myers Squibb Co.** CEO Giovani Caforio, **Merck & Co. Inc.** CEO Kenneth Frazier, and **AbbVie Inc.** CEO Richard Gonzalez.

BRINGING IDEAS TO THE TABLE

Several leaders included ideas for lowering drug costs in their opening statements. Soriot's opening testimony stood

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BROUGHT TO YOU BY THE EDITORS OF **PHARMASIA NEWS, START-UP** AND **SCRIP INTELLIGENCE**

Roche Swallows Spark

$4.8bn buy shores up Swiss firm's position in gene therapy and hemophilia (p5)

Scrip's SMA Guide

Sales, development and launch plans map out spinal muscular atrophy field (p12)

Brexit D-Day Looms

UK government outlines plans to avoid supply disruptions in no-deal scenario (p19)

from the editor

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Last week I wondered about gene therapies, and their apparent resistance to the rule whereby the price of a technology comes down as it is taken up more widely. In light of that discussion around the pricing of the products, it is interesting to consider the price of gene therapy companies themselves.

When Novartis acquired AveXis less than a year ago, it paid nearly $9bn. We now see Roche paying just under $5bn for Spark Therapeutics, which unlike AveXis already has a product on the market, even if its pipeline is less well advanced (see p5-6). A few days later, Biogen has agreed to buy Nightstar Therapeutics in a deal worth about $800m, for which it gets a lead asset in Phase III and others further back in development.

With 2019 shaping up to be an important year for gene therapy in terms of trial data and product approvals, there will undoubtably be more acquisitions by the big players of the smaller pioneers in the field. Although competition can push up prices, the increasing pervasiveness and advancing maturity of gene therapy firms may mean that buyers can afford to be choosier and push to get more for less, particularly as more big companies are building experience in the area.

Aside from outright acquisitions, gene therapy partnerships continue afoot. See p15 for details of AbbVie's collaboration with Voyager Therapeutics, which aims to deliver a gene therapy through the blood-brain barrier as a one-time treatment for Parkinson's disease.

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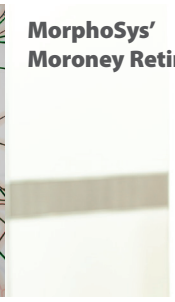

exclusive online content

Another Botox Competitor: Revance Prepares Longer-Lasting RT002 For BLA Submission

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CEO Dan Browne insists that **Revance Therapeutics Inc.**'s technology is the first innovation in neuromodulators in 30 years, providing a longer-lasting botulinum toxin-based injection for aesthetic and therapeutic uses than the four approved products in this category, including **Allergan PLC**'s market-leading blockbuster *Botox* (onabotulinumtoxinA).

Revance's claim that lead product candidate RT002 (daxibotulinumtoxinA) can beat the three-to-four-month duration of efficacy of existing neurotoxins by two months will be reviewed by the US FDA later this year after the company submits a biologic license application (BLA) seeking approval to treat glabellar lines – frown lines appearing between and above the eyes – with dosing as infrequent as every six months. The filing is expected to take place in the first half of 2019 following positive results from Revance's third Phase III study SAKURA 3 in December.

Scrip spoke with Browne about the data and the company's strategy for RT002 while in San Francisco for the J.P. Morgan Healthcare Conference in January, including the company's plans for developing the neuromodulator for both aesthetic and therapeutic indications, and its separate partnership with **Mylan NV** for a Botox biosimilar, which the FDA could allow to move forward this year.

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To read the rest of this story go to: https://bit.ly/2NHDkTu

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out in that regard, with four clear-cut proposals, including rebate reform, out-of-pocket caps for Medicare patients, a system that supports value-based agreements, and fostering a healthy biosimilar market.

All seven leaders voiced strong support for reforming the current rebate system. Some, like Pfizer's Bourla, pledged to return the savings from rebates to patients. "We commit that every single dollar will go to the patients," Bourla said.

He also advocated for policy changes that would pave the way for rebate reform in Medicare and commercial plans, which he said would result in lower list prices.

Merck's Frazier echoed that sentiment, claiming rebate changes would need to occur across both commercial and government plans before he could commit to lower list prices.

"Assuming that we do change the systems on the commercial side and the Medicare side so that no one company faces a disadvantage, we would be lowering list prices," Frazier said. "We have lowered list prices in the past and have found that it creates a financial disadvantage for the company and it doesn't get us more volume because of the incentives in the system."

Ranking Member Ron Wyden (D-Ore.), who delivered some of the more confrontational statements in his opening remarks – calling out the industry for empty gestures on pricing – wanted something more official. He demanded that each of the leaders respond in writing within 10 days as to whether or not they would support a law requiring list price reductions by the amount of the rebate if rebates are eliminated.

There were other confrontational moments, like when Sen. Maggie Hassan (D-N.H.) grilled Taubert on Johnson & Johnson's opioid marketing practices. Hassan's line of questioning was raw, but Taubert was able to deflect by pointing out that opioid sales account for less than 1% of J&J's current revenues.

REPUBLICANS PLAY TOUGH

Some of the most surprising and challenging lines of questioning came from Republican senators, particularly Sen. Bill Cassidy (R-La.). "It is almost as if the taxpayer has stupid written on their face," he said, holding up packaging for *Duexis* (ibuprofen/famotidine), a combination of two drugs available generically and manufactured by **Horizon Pharma AG**, which he said costs more than $200 a month.

"We have lowered list prices in the past and have found that it creates a financial disadvantage for the company and it doesn't get us more volume because of the incentives in the system."

Cassidy almost seemed to be advocating in favor of direct Medicare negotiations at one point. "Medicare has a very limited ability to negotiate based on marginal value, and I think that is one of the fundamental problems in this," he said. "Is it reasonable if Medicare should have the ability to make some sort of judgement based on the relative value of the medicine?" he asked.

Taubert took a stab at answering, noting, "The PBMs are very effective in negotiating. We don't know that the government would be as effective at negotiating as the professional negotiators."

Cassidy turned his line of questioning to the high cost of drug prices compared to other countries, and HHS' proposed rule to develop an international pricing index for some drugs under Medicare Part B. *(Also see "Medicare IPI Model Could Import Benefit Of Biosimilar Competition, Azar Suggests" - Pink Sheet, 15 Jan, 2019.)*

"Something is fundamentally broke in our system that the Danes get an 80% discount and we are not," Cassidy said.

Pharma was also grilled by Wyden about whether or not they make a profit in other Western industrialized countries, where the drugs are priced substantially lower, to which they testified that they do. "We make money in any country in which we sell unless we donate the product," AbbVie's Gonzalez testified.

But the industry leaders tried to counter that new drugs are not always available in other markets the way they are in the US. Bourla quietly responded with one zinger, "I can assure you if you get cancer or another serious disease, you want to be treated in this country."

They were also asked if they've reconsidered their international pricing strategies, to which Frazier responded, "The reality of the world is the greatest opportunity we have is to walk away … and frankly, they know that."

Pfizer's Bourla and AbbVie's Gonzalez both advocated in favor of the US exploring trade agreements as a way to better balance the differential pricing around the world.

Sen. John Cornyn (R-Texas) took a deep dive into AbbVie's patent estate around *Humira* and a line of questioning around the delayed launch of biosimilar versions of Humira in the US versus Europe. Then, he suggested the Senate Judiciary Committee take up a review of the patent issues, which Grassley said he would support.

A Senate Judiciary inquiry could open up a whole new line of Congressional oversight that industry would surely prefer to avoid.

But by the end of the hearing only Grassley and Cassidy were left for the closing remarks, not exactly an intimidating audience for the polished group of pharmaceutical executives. The meeting was called to a close, and there was a collective sigh of relief from the industry.

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Roche $4.8bn Buy Sparks Hemophilia Gene Therapy Race

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Roche is buying gene therapy specialist **Spark Therapeutics Inc.** for $4.8bn to get hold of the latter's already approved Luxturna for inherited blindness and a pipeline that contains a couple of potential hemophilia A treatments that will boost the Swiss major's presence in the rare blood disease space.

The Basel-based company is splashing out $114.50 per share to acquire Spark, representing a premium of 122% on the US biotech's closing price on Feb. 22 and 19% more than its 52-week high share price on July 9, 2018. The deal is set to close by the end of the second quarter and Spark will continue its operations in Philadelphia – it was founded in March 2013 out of two decades of gene therapy research at Children's Hospital of Philadelphia – as an independent company within the Roche group.

Spark was the first company to receive FDA approval for a gene therapy for a genetic disease in Dec. 2017, when *Luxturna* (voretigene neparvovec) got the nod as a one-time treatment for the rare eye disease biallelic RPE65 mutation-associated retinal dystrophy. It is currently marketed in the US by Spark, launched with a price tag of $850,000, and by Roche rival **Novartis AG** in Europe where it was granted marketing authorization in November last year. *(Also see "The First US Gene Therapy Maker Innovates On Pricing And Reimbursement" - Scrip, 3 Jan, 2018.) (Also see "Luxturna Approved In EU: Novartis Outlines Lessons For Gene Therapy Strategies" - Scrip, 23 Nov, 2018.)*

However, most of the excitement centers around Spark's investigational gene therapies for hemophilia A, an area that Roche entered at the end of 2017 with the approval of *Hemlibra* (emicizumab). The latter has got off to a strong start, with fourth quarter sales topping CHF100m, helped by an additional approval in the US last year that means it is cleared for patients with and without inhibitors to Factor VIII. *(Also see "Roche's Hemlibra Wins Expanded FDA Approval, Opening The Door To Broad Hemophilia A Opportunity" - Scrip, 4 Oct, 2018.)*

Spark's lead clinical asset is SPK-8011, a gene therapy for hemophilia A, which is expected to start Phase III in 2019 this year. It also is developing SPK-8016 in a Phase I/II trial aimed at addressing the hemophilia A inhibitor population.

The deal has gone down well with the investment community with most believing that a gene therapy that gets to market will not cannibalize Hemlibra sales and given the likelihood that not all hemophilia A patients could be treated with gene therapy, there is a room for both types of treatments. Morgan Stanley analysts issued a note saying that SPK-8011 will complement the Hemlibra franchise, "which is expected to remain a cornerstone of therapy," while the team at Credit Suisse wrote a note saying that the deal suggests that "big pharma views hemophilia A as a significant value driver," as it is the second recent acquisition in the

field, following **Sanofi**'s $11.6bn purchase of **Bioverativ Inc.** last year. *(Also see "Ablynx, Bioverativ Buys Drive Sanofi's Hematology Reign" - Scrip, 29 Jan, 2018.)*

Credit Suisse went on to note that "the implication of this trend bodes especially well for the risk-reward in 2019 for **BioMarin Pharmaceutical Inc.**." The broker believes that the latter's Phase III candidate valoctocogene roxaparvovec (also known as BMN 270 or val-rox) "currently holds a first-mover position among hem A gene therapies in development with a 1.5 year-plus potential lead to market" and BioMarin, long touted as a takeover target, could be next to go under the hammer, as well as other gene therapy companies such as **Sarepta Therapeutics Inc.**, **Ultragenyx Pharmaceutical Inc.**, **PTC Therapeutics Inc.** and **Solid Biosciences Inc.**.

Analysts at Deutsche Bank said that the deal hedged Roche's efforts in hemophilia, allowing it to grow Hemlibra "and be part of the next big thing that could be around the corner in this fast-paced environment." The acquisition "may add extra concern on the long-term dynamics of the market for Hemlibra, but at the same time reassures that Roche could be part of this change," they added. *(Also see "Hemophilia Seen As Good Testing Ground For Commercializing Gene Therapy" - Scrip, 8 Oct, 2018.)*

Roche also stressed that there was more to Spark's pipeline than hemophilia A. Its other assets include SPK-9001, an investigational gene therapy being developed with **Pfizer Inc.** for hemophilia B which is in Phase III and SPK-7001 for choroideremia, currently in Phase I/II trials. The company is also developing SPK-3006 for Pompe disease and SPK-1001 for CLN2 disease – a form of Batten disease – which are expected to be ready for clinical development in 2019, as well as additional preclinical programs for Huntington's disease and Stargardt disease.

The Morgan Stanley analysts added that the deal gave Roche "a leading seat at the table in the emerging field of gene therapy." The programs acquired fit with the company's expanding focus in rare diseases and neuroscience, "therapeutic areas typified by high innovation risk and low commercial risk," they said, going on to compare the deal with Novartis' acquisition of **AveXis Inc.** for $8.7bn in April 2018 to accelerate its own in-house gene therapy effort; the firm gained access to a more advanced lead asset –*Zolgensma* for spinal muscular atrophy, "but arguably a less rich, diverse pipeline," the broker wrote. *(Also see "Novartis Pharma CEO Sees Zolgensma Supplanting Spinraza" - Scrip, 1 Feb, 2019.)*

The proposed deal also got the thumbs-up from Jefferies with the broker noting that Roche is acquiring "existing gene therapy manufacturing capacity and expertise." It added that Spark also offered experience and know-how regarding chemistry, manufacturing and controls, validation, assay work "and other unique skill sets different than traditional drug approvals."

The Deutsche Bank team also went with the 'seat at the table' image if gene therapy changes the paradigm, claiming that the proposed Spark acquisition "alleviates the threat of competition in areas where Roche could conceivably have faced longer-term threats to its current late-stage pipeline." The analysts point out that Spark's intellectual property suite, particularly around adeno-associated virus vectors "likely means that not only is Roche well advanced in gene therapy, but it can also benefit (from royalties) from future competitive therapies wanting to utilize the technology."

They concluded by saying that the deal, which is "small change for Roche," gives the latter "one of the most advanced companies in the field and allows it to leapfrog the initial time and investment normally required."

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Celgene/BMS: Happy Union Or Runaway Bride?

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With **Bristol-Myers Squibb Co.**'s largest institutional investor revealing that it opposes the $74bn acquisition of **Celgene Corp.** and a recently engaged activist investor trying to build a strong case against the combination, several analysts nonetheless say the proposed deal – facing an April 12 shareholder vote – still has sufficient momentum to go through.

Questions surrounded BMS's intent to acquire Celgene at a 54% premium to its closing price Jan. 2 closing of $66.64. The terms unveiled Jan. 3 also give Celgene upside potential in the form of a $9 contingent value right (CVR) pegged to approval of three late-stage Celgene pipeline assets. *(Also see "Bristol Values Celgene's Hematology, Immunology Portfolio At $74bn, But Does It Price In Risk?" - Scrip, 3 Jan, 2019.)* Celgene's stock price had been declining because of several regulatory and clinical setbacks. In that regard, BMS is taking advantage of the opportunity, but some investors are still questioning the size of the premium.

On Feb. 27, Wellington Management, which owns 7.7% of BMS's outstanding stock according to a Schedule 13D filing with the US Securities and Exchange Commission (SEC), issued a terse press release stating that it does not support the proposed merger for three reasons.

1. The deal places too much risk on BMS shareholders and gives Celgene shareholders significant equity in the combined company at a discount.
2. The merger's execution could be more challenging than portrayed by the principals.
3. There could be "alternative paths" to value creation that would benefit BMS shareholders more.

Wellington is the largest institutional shareholder in BMS, so its opinion carries weight, even if it holds voting control over slightly more than 20% (more than 28.1m shares) of the total outstanding company stock it owns (nearly 125.7m shares). There are more than 1.6bn general shares in BMS in circulation presently. Reports suggest that BMS's fifth-largest institutional shareholder, Dodge & Cox, also opposes the merger but it has not said so publicly.

Adding to the refrain on Feb. 28 was a 16-page letter against the transaction from activist investor Starboard Value LP, which holds about a 1% ownership in BMS, obtained almost entirely since the Celgene deal was announced in early January. Starboard nominated five of its own executives, including CEO Jeffrey Smith, as board members in BMS, but a vote on those candidacies would not occur before the April shareholder vote on the merger.

STARBOARD ALLEGES BMS MOVED DEFENSIVELY, HASTILY

Starboard's argument against the merger, while much longer than Wellington's, made similar arguments. Mainly, the group says BMS essentially would be buying a ruinous patent cliff as Celgene's top-selling drug, hematologic cancer therapy *Revlimid* (lenalidomide), accounts for 63% of the big biotech's sales revenue but faces US patent expiration in 2022.

Starboard further posits that BMS hurried into a merger with Celgene from a defensive posture – seeking to stave off acquisition by a third party – and assumed highly optimistic prospects for Celgene's R&D pipeline to make the financials seem attractive.

"There is a better path forward for Bristol-Myers, either as a more profitable standalone company with a more focused, lower-risk strategy, or in a potential sale of the whole Company," the letter states.

The activist investor said that it approached analysis of the proposed deal with an open mind and a willingness to be persuaded of its benefits, taking numerous meetings and calls with BMS execs. The letter concludes that "the more work we do, the more conviction we build that this transaction is not in the best interest of shareholders. Therefore, we intend to solicit shareholders to vote against the transaction." It adds that its views are "solidified" by "numerous other long-term shareholders" in BMS who also oppose the deal.

To work financially, BMS apparently believes that Celgene's pipeline can yield new products replacing more than 60% of current revenue in the next seven years, which Starboard says "is an aggressive assumption and may not be realistic based on historical precedents." Further, it alleges that BMS performed only about two weeks of due diligence regarding Celgene's R&D potential, which would seem insufficient to evaluate a set of candidates expected to produce significant near-term revenue.

"There is a better path forward for Bristol-Myers, either as a more profitable standalone company with a more focused, lower-risk strategy, or in a potential sale of the whole Company," the letter states.

Starboard's assertion that BMS's decision to acquire Celgene was "hastily construed" ignores the fact that the two companies mutually considered a merger for several weeks in mid-2017, meaning there had been prior due diligence. In SEC filings, BMS revealed that it had been an off-and-on suitor for Celgene for more than a year and a half, during which time Celgene sought out another large pharma – possibly **Merck & Co. Inc.** – as a potential buyer but was rebuffed.

TOO MUCH CROSSOVER OWNERSHIP TO SCUTTLE MERGER

In a Feb. 28 note, BMO Capital Markets analyst Alex Arfaei called some of Starboard's rationale "simplistic, and arguably overstated or misleading." Nonetheless, the charge that BMS made a hasty, defensive decision to go forward with its bid for Celgene is serious and something that BMS management needs to get out ahead of with a direct response, the analyst added.

Arfaei conceded that BMS's posture in seeking to acquire Celgene was partly defensive, although he thinks the company is hedging as much against internal risk as against the possibility of being acquired by another company. With its recent R&D setbacks in immuno-oncology and the increasing probability that *Opdivo* (nivolumab) will fail to obtain labeling for first-line non-small cell lung cancer (NSCLC), the diversification beyond IO that acquiring Celgene would provide has a clear rationale, Arfaei said.

He added that Wellington and Starboard's now-public opposition to a BMS/Celgene tie-up indicates that both shareholders perceived an increased likelihood of better valuation from a third-party buyout of BMS. Nonetheless, given the significant overlap in BMS and Celgene stock ownership – BMO estimates it as "at least 35%" while Michael Yee of Jefferies estimates 25% material overlap – the merger is still very likely to obtain enough votes for approval, Arfaei asserted.

Yee argued in a Feb. 28 note that overlapping shareholders would have too much to lose by opposing the deal, noting the appreciation in Celgene stock value since the planned merger was announced. Celgene closed the trading day Feb. 28 down 8.7% to $83.06 per share, reflecting increased uncertainty about the merger vote, while BMS closed up 1.4% to $51.66.

"If the deal is voted against, then Celgene stock would fall significantly, possibly to the 'pre-deal' price around $65 or even lower, and funds that own Celgene thus would experience significant downside losses if the deal doesn't happen," Yee said. Many BMS shareholders who don't like the proposed deal probably voted with their feet already and sold off their positions, he pointed out.

In a Feb. 27 note that circulated shortly after Wellington's announcement but before the Starboard letter's release, Tim Anderson of Wolfe Research commented that investor sentiment toward the merger is mixed, with holders just of BMS shares less positive on the deal on than those who hold positions in BMS and Celgene or just Celgene. Still, Anderson said the survey suggested the odds of a third party coming in and buying BMS before the April 12 vote at just between 10%-20%, an estimate Wolfe Research agrees with.

"Survey respondents still tilted in favor of voting for the deal," Anderson noted. "Even if we assume that firms who solely (or mostly, as in the case of Wellington) own BMS shares vote against the transaction, about two-thirds of remaining shareholders appear to have meaningful stakes in both companies, which suggests a majority will still vote in favor of deal closure. However, aggressive shareholder activism – or a change in circumstances such as a bidder (e.g. **Amgen Inc.**) coming in for BMS – could still be disruptive."

In a recent assessment of M&A possibilities among the large pharma companies, Morningstar determined that even after the Celgene acquisition went through, BMS might remain an appealing and realistic takeout target for **Pfizer Inc.** or **Johnson & Johnson**. For **Sanofi**, **Novartis AG**, Amgen, **AbbVie Inc.** and **Gilead Sciences Inc.**, buying BMS would make sense strategically, but would be beyond their financial means once Celgene was incorporated into the valuation.

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Triple Threat: Full Rhinosinusitis Data Place Dupixent Top Of The IL Heap

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Positive full data from the Phase III trials of *Dupixent* (dupilumab) in severe chronic rhinosinusitis with nasal polyps (CRSwNP) mean that the drug could be the first in its class to have three indications, giving it a significant advantage over anti-interleukin rivals *Fasenra* and *Nucala*, currently approved only in asthma.

These results will allow **Sanofi** and **Regeneron Pharmaceuticals Inc.** to file a dossier with the regulators very soon. Already approved in atopic dermatitis and moderate to severe asthma, approval in this new indication would give anti-IL-4 antibody Dupixent clear market dominance over **AstraZeneca PLC**'s Fasenra (benralizumab) and **GlaxoSmithKline PLC**'s Nucala (mepolizumab), both IL-5 inhibitors, as about 30% of patients with severe asthma also suffer from atopic dermatitis and nasal polyps.

The SINUS-24 and SINUS-52 trials demonstrated that when dupilumab was added to the standard-of-care corticosteroid nasal spray it improved nasal polyp size, nasal congestion severity, chronic sinus disease, sense of smell and co-morbid asthma outcomes.

In these severe patients, Dupixent reduced the need for systemic corticosteroid use and the need for nasal/sinus surgery. Top-line results from the trials were announced in October, showing a 57% and 51% improvement in nasal congestion/obstruction severity compared with a 19% and 15% improvement with placebo in SINUS-24 and SINUS-52. These newly released full data, announced at the Annual Meeting of the American Academy of Allergy, Asthma & Immunology (AAAAI) in San Francisco, rounded out details on Dupixent's applicability and efficacy in CRSwNP, showing that treatment effects began as early as four weeks with progressive improvement up to 24 weeks in SINUS-24, a 24-week trial, and up to 52 weeks in SINUS-52.

NEW DATA POINTS

Head of clinics of the Department of Oto-rhinolaryngology at Ghent University and principal investigator of the trial, Claus Bachert, said that: "Patients with co-morbid CRSwNP and asthma are often more difficult to treat so it is encouraging that Dupixent, which targets key drivers of type 2 inflammation, may address both conditions in these patients."

There was a reported 0.21L improvement in lung function versus placebo at 24 weeks in SINUS-24 in the subset of patients with asthma at baseline and 0.21L improvement in lung function versus placebo at 24 weeks in SINUS-52. In the trials, approximately 60% of patients had co-morbid asthma, most of them receiving asthma controller medication.

New data also showed a 42% and 27% improvement in sinus opacification vs. 4% and 0% with placebo at 24 weeks in SINUS-24 and SINUS-52, respectively. At 52 weeks in SINUS-52, a 37% improvement in sinus opacification was achieved with Dupixent treatment vs. 2% with placebo.

There was a 146% and 108% improvement in ability to identify different smells versus 19% and 7% with placebo at 24 weeks in SINUS-24 and SINUS-52, respectively. In both trials, Dupixent-treated patients reported an improvement in sense of smell as early as four weeks based on a separate daily assessment.

John-Jacques Le Fur, analyst at Bryan, Garnier & Co, said that the most interesting parameter in the trials results was the was the reduction in rescue treatment (systemic corticosteroids or nasal polyp surgery) with 73% reduction at week 24 and 76% reduction at week 52. "Nasal polyps are difficult to treat since in most of the cases surgery is ultimately needed without full success," he said.

Current treatments for CRSwNP include intranasal corticosteroids, systemic corticosteroids and surgery, which often has suboptimal efficacy and/or high recurrence rates after treatment. After treatment, patients may experience severe nasal obstruction with breathing difficulties, nasal discharge, reduced or loss of sense of smell and taste and facial pain or pressure.

Bryan, Garnier & Co estimated that Dupixent has sales potential of around €750m ($852m) in 2025 for this indication alone, and forecasts global sales of the drug to be €6.1bn ($6.9bn) the same year. Just in asthma, *Datamonitor Healthcare* forecasts that Dupixent to be the highest grossing IL biologic, with 2026 sales of $1.8bn across the US, Japan, and five major EU markets.

IL CLASS SHIFT?

Datamonitor Healthcare analysts explain that while the "lack of head-to-head trials between biologics makes direct comparisons of efficacy and safety challenging, Dupixent has data suggesting greater comparative improvements in lung function in difficult-to-treat patient groups versus the IL-5 inhibitors."

With this full data set on the table, Sanofi and Regeneron could steal a march on others in the IL inhibitor class. However, competitors are making moves that could, in time, claw back some of the market.

AZ's Fasenra is currently being evaluated in a 400-patient Phase III study in severe nasal polyposis that began in January 2018, and is due to complete in November 2020.

Further down the line is GSK's biologic Nucala, also in a 400-patient Phase III trial for severe nasal polyposis and hypereosinophilic syndrome, which began in June 2017 and was expected to report data in 2018, but has been delayed until the first half of 2020. Nucala trials in atopic dermatitis and esophagitis have been suspended.

In a 2018 interview with *Scrip*, Regeneron CEO Len Schleifer said he believed that with dupilumab, the companies will have "changed allergic diseases and how they are thought of, and treated, forever."

Regeneron is now testing the antibody in different settings such as food allergies, pollen allergies and allergies of the esophagus. "We really think that we have hit upon this fundamental driver essentially for all allergic disease," Regeneron CSO George Yancopoulos told *Scrip*, calling allergies the "major scourge and epidemic of modern society."

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Daiichi Sankyo Realigns Japan R&D As Oncology Comes To Fore

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In line with an increased focus on its oncology operations, which are now moving towards commercialization, **Daiichi Sankyo Co. Ltd.** is realigning its R&D activities in Japan and taking other steps to support anticipated growth in the sector.

Amid sliding sales for its former top product, the blockbuster antihypertensive olmesartan, and the strategic push into oncology, the company will from April organize its research functions in Japan along pharmacology and "synthesis function" lines.

The operations have so far been aligned with specific therapeutic areas, but with the stronger focus on the cancer pipeline, the restructuring is designed to improve efficiency and "strengthen the R&D system centered on oncology," the Japanese company said.

In contrast to peers such as **Takeda Pharmaceutical Co. Ltd.**, Daiichi's main R&D activities globally remain relatively concentrated in Japan, where it has four major sites, although global clinical trials are overseen from a New Jersey, US site. 2011 acquisition **Plexxikon Inc.** in California is focused on structure-guided small molecule oncology drugs, and a German site from another purchase, **U3 Pharma AG**, currently acts as a tissue and cell research center.

OTHER CHANGES

In other moves aimed at accelerating the oncology pipeline, pharmacological research functions in Japan will also be spread across two main oncology research laboratories, honing the broader biologics and immuno-oncology function of one of the facilities.

Former specialty medicine functions in areas such as rare diseases and pain and neuroscience will also be reorganized from April into two specialty medicine research labs, with small molecule synthesis research consolidated into a newly established medicinal chemistry research lab.

A new clinical department to manage the manufacture and provision of supplies of investigational products for global clinical trials, and a dedicated chemistry, manufacturing and control regulatory affairs department.

Again in support of anticipated oncology approvals, certain supply chain functions will be reorganized, and a new medical science department in oncology set up to provide medical affairs support.

The changes are the latest in a string of restructuring moves at Daiichi Sankyo

over the past few years, which have also been prompted in part by the global genericization of angiotensin 2 antagonist olmesartan, sold as *Benicar* and *Olmetec* and in various combinations.

Total global sales of this product family slumped by 33% in the fiscal nine months to Dec. 31, hastening the need for the strategic push into oncology.

Other restructuring steps have included divestment of selected assets in Japan such as manufacturing facilities and older drugs, job losses in the US, and the dissolution this year of the **Japan Vaccine Co. Ltd.** joint venture with **GlaxoSmithKline PLC**.


Daiichi Aims Big In Oncology

ONCOLOGY AMBITIONS

The oral FLT3 inhibitor quizartinib – acquired in the $410m buyout of US venture **Ambit Biosciences Inc.** in 2014 – is spearheading Daiichi's oncology ambitions. The molecule was filed last November in the US, where it has a priority review and Breakthrough Therapy designation for FLT3-ITD-positive relapsed/refractory acute myeloid leukemia.

It was also submitted in Japan and the EU around the same time for this indication, and is in Phase III for first-line use.

Analysts also view the antibody-drug conjugate trastuzumab deruxtecan (DS-8201) as another key mid-term growth driver, now in Phase III for HER2-positive breast cancer. The therapy links an HER2-targeting antibody with a topoisomerase I inhibitor to provide targeted delivery.

Although Daiichi last year delayed its mid-term financial targets, at the same time it said it was planning to raise overall R&D spending by JPY200bn over the same time frame ($1.8bn; see side bar).

In total, it is aiming for JPY500bn in revenues from the oncology sector in fiscal 2025, from a base of almost nothing at present, supported by the planned rollout of seven new molecular entities over the 2018-25 period.

EDOXABAN TOP IN Q3

The company reported a 5% fall in revenues to JPY703.1bn in the fiscal nine months to December 31, although operating profit was up by 4% to JPY97.1bn.

The oral direct Factor Xa inhibitor anticoagulant edoxaban, sold as *Lixiana*, *Effient* or *Savaysa*, led the charge, growing by 54% globally to JPY87.4bn in the period, making it Daiichi's top product.

Olmesartan products meanwhile fell to JPY80.9bn, and are expected by the company to slide by 35% in the full fiscal year.

In a note on the "relatively favorable" results, Morgan Stanley Japan analyst Shinichiro Muraoka said he was "watching closely" whether DS-8201 will be granted US accelerated approval for breast cancer around late April.

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From the editors of PharmAsia News.

AZ Lynparza Head Hopes 2020 Will See PARP Inhibitor Treating Pancreatic Cancer

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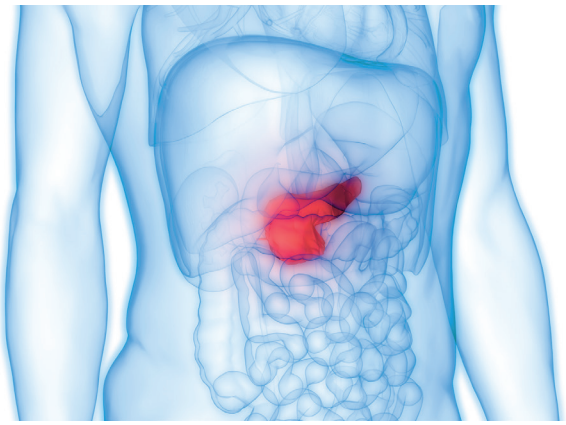
AstraZeneca PLC and **Merck & Co. Inc.** will soon initiate talks with regulators after their breast and ovarian cancer drug *Lynparza* (olaparib) cut the risk of disease progression or death as a first-line maintenance treatment in germline BRCA-mutated metastatic pancreatic cancer. If all goes well the PARP inhibitor will have its third indication in by 2020, according to Greg Rossi, global medicines lead for Lynparza at AstraZeneca.



POSITIVE POLO

He was speaking to *Scrip* after Lynparza, which is currently being used as treatments for ovarian and breast cancer, showed itself in the Phase III POLO trial to be better at preventing gBR-

CAm metastatic pancreatic cancer from worsening when compared with a placebo.

Topline data from the trial, announced Feb. 25, showed a statistically significant and clinically meaningful improvement in progression-free survival (PFS) with Lynparza versus placebo. The safety and tolerability profile of Lynparza was consistent with previous trials, the companies said.

Lynparza is a first-in-class PARP inhibitor and the first targeted treatment to block DNA damage response in cells/tumors harboring a deficiency in homologous recombination repair (HRR), such as mutations in BRCA1 and/or BRCA2.

Inhibition of PARP with Lynparza leads to the trapping of PARP bound to DNA single-strand breaks, stalling of replication forks, their collapse and the generation of DNA double-strand breaks and cancer cell death.

"We thought that the biology associated with DNA damage repair and some of the early data that we had seen in studies gives an indication that at least in BRCA patients there could be benefit from Lynparza," Rossi explained. Patients with BRCA gene mutation represents between 5% and 7% of pancreatic patients.

Patients in the randomized POLO trial started receiving Lynparza after around 16 weeks of having had platinum chemotherapy.

"We moved patients then to a maintenance treatment with Lynparza, which produced a statistically significant result. The primary endpoint was progression-free survival. We treated the patient until the point of disease progression," Rossi said.

He did not reveal for how long the patients remained progression-free. That will be revealed with full results of the trial at an undisclosed medical meeting later this year.

"We will now have conversations with regulators over the next few weeks to see if we can get a licensed new use for Lynparza as a treatment for pancreatic cancer," he said in an interview.

LYNPARZA LOOKS SET FOR PANCREATIC CANCER STATUS

"Our typical timelines for a supplemental indication review by regulators is something like a year, perhaps a little less. So, we would hope to have a new use for Lynparza in 2020 [as a treatment for pancreatic cancer]," Rossi said.

"There is a very big unmet medical need in pancreatic cancer and the regulators are very aware of that unmet need. We are committed to making this treatment available to pancreatic cancer patients. We will discuss any opportunity to move this quickly," he added.

Lynparza already leads the PARP inhibitor class across all tumor types with more than 50% total patient share.

Other PARP Inhibitors include **Pfizer Inc.**'s *Talzenna* (talazoparib), **Clovis Oncology Inc.**'s *Rubraca* (rucaparib) and **Tesaro Inc.**'s (acquired by **GlaxoSmithKline PLC** in Dec 2018) *Zejula* (niraparib).

AstraZeneca's Rossi said results from the POLO trial trial "positions us as the pioneer in pancreatic cancer. We are now the only PARP inhibitor now with poster Phase III data in three independent tumors, those being breast, ovarian and pancreatic."

> "We would hope to have a new use for Lynparza in 2020 [as a treatment for pancreatic cancer]." - AstraZeneca Lynparza global program head Greg Rossi

OTHER TUMOR TYPES TARGETED TOO

Lynparza is being tested in a range of PARP-dependent tumor types with defects and dependencies in the DDR.

"We have a pretty broad program for Lynparza. We have ongoing Phase III programs as monotherapy in prostate, but also have a series of combination trials. They include in prostate cancer, ovarian but also in bladder cancer, and in non-small cell lung cancer," Rossi said.

"Our combination experiments will allow us to move into other tumor types so potentially outside of DDR gene mutation groups. So within DNA damage response we're looking at a series of genes that are highly implicated in DNA damage repair pathways, of which BRCA are an archetypal DNA damage repair gene, but there are a range of other genes that are really interesting and maybe just as important in repairing DNA damage. And we think that Lynparza could easily work in patients that have got mutations in those gene pathways."

"The takeaway from the POLO trial is that it shows the power of Lynparza."

"If we in pancreatic cancer show that we've got a clinical effect – and as we expand beyond breast and ovarian cancer – it gives us renewed confidence about the potential for this molecule in multiple tumor settings," Rossi concluded.

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SCRIP'S GUIDE TO

Spinal Muscular

THE FRONT RUNNERS

Spinraza

APPROVED

Biogen's intrathecal antisense oligonucleotide is the only approved drug for SMA

DISEASE OVERVIEW

» **Spinal muscular atrophy** (SMA), which affects one in 10,000 live births, causes progressive muscle weakness and loss of movement and is caused by defects in the survival motor neuron 1 (SMN1) gene that encodes the SMN protein. This protein is needed for the health and survival of nerve cells in the spinal cord responsible for muscle contraction.

» **All patients retain a "back-up" gene,** SMN2, which produces some SMN protein. However, this is mostly non-functional and cannot fully make up for the faulty SMN1 gene. The number of copies of SMN2 varies from person to person, from 0-8. Having more SMN2 copies is generally associated with less severe SMA symptoms.

» **Treatment approaches include gene therapy** to replace the faulty SMN1 gene, modulation of SMN2 splicing via antisense oligonucleotides or small molecules to induce SMN2 to produce more functional SMN protein, and seeking to protect or enhance neurotransmission or muscles.[1]

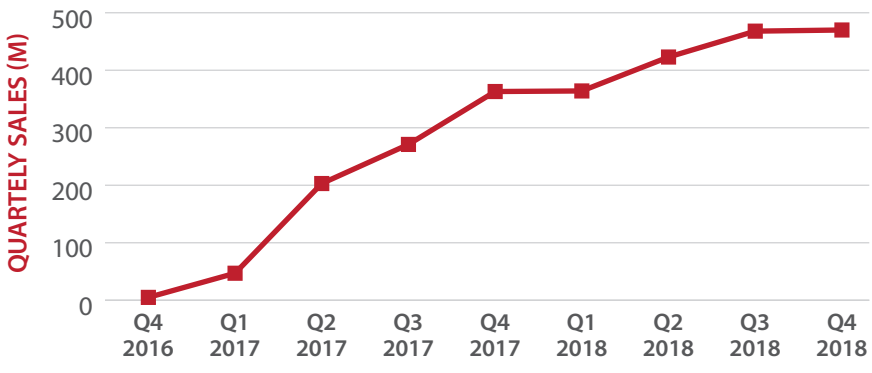
> *"The Spinraza clinical trial program has included more than 300 patients followed up for up to six years.[2]"*
>
> **– Michael Ehlers, VP of R&D, Biogen**

SPINRAZA SALES

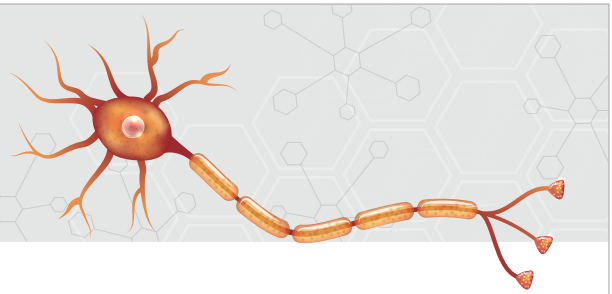
2016 $5m

2017 $884m

2018 $1,724m



Atrophy Therapies



APPROVAL DECISION EXPECTED 2019

Zolgensma

Novartis' gene therapy is expected to be approved by US FDA in H1 2019 and has potential to dominate the market, but question remains over duration of effect, particularly when given to babies.

"If we get the right label and it's broad enough for use in presymptomatic patients there's no point in the other mechanism.[3]"

– Paul Hudson, CEO, Novartis Pharmaceuticals

APPROVAL DECISION EXPECTED 2020

Risdiplam

Roche's oral splicing modulator is scheduled for mid-2019 filings for 2020 approval target and has more convenient oral dosing compared with intrathecal Spinraza.

"There is almost certainly a place for molecules next to gene therapy…[4]"

– Severin Schwan, CEO, Roche

DRUG AND PIPELINE OVERVIEW[5]

Drug	Phase	Likelihood of Approval*	Company	Population	Therapeutic Approach	Route of Administration	Dosing
nusinersen (Spinraza)	Launched	100%	Biogen/Ionis Pharmaceuticals	Types 1, 2 and 3	SMN2 splicing modifier	intrathecal	4 loading doses then once every 4 months
onasemnogene abeparvovec (Zolgensma)	Pre-registration	99%	Novartis/Regenxbio/ Genethon	Filed for Type 1, also in development for 2 and 3	SMN1 gene replacement	intrathecal and iv	one time
valproate sodium	Phase III	n/a	Kowa Pharmaceutical	Types 1, 2 and 3	SMN2 splicing modifier, neuroprotection	oral	n/a
risdiplam	Phase II/III	29%	Roche/PTC Therapeutics	Types 1, 2 and 3	SMN2 splicing modifier	oral	once daily
branaplam	Phase II	62%	Novartis	Type 1	SMN2 splicing modifier	oral	once weekly
amifampridine phosphate (Firdapse)	Phase II	24%	Catalyst Pharmaceuticals/ Jazz Pharmaceuticals/ BioMarin	Type 3	Neuromuscular junction transmission enhancement	oral	n/a
reldesemtiv	Phase II	25%	Cytokinetics/ Astellas Pharma	Types 2, 3 and 4	Muscle enhancement	oral	twice daily
BIIB110	Phase I	16%	Biogen/AliveGen	not-specified	Muscle enhancement	Unknown	n/a
SRK-015	Phase I	16%	Scholar Rock/ Johnson & Johnson	Types 2 and 3	Muscle enhancement	intravenous	n/a
BIIB089	Phase I (Clinical Hold)	16%	University of Pennsylvania	not specified	SMN1 gene replacement	unknown	n/a

*Calculated by Biomedtracker based on disease group and development phase baseline and analyst opinion subjective score

Spinal Muscular Atrophy Therapies

COSTS

» $750,000

US list price for Spinraza in first year, $375,000 per year thereafter.

Spinraza pricing has limited its availability in some markets.

» $4-5m

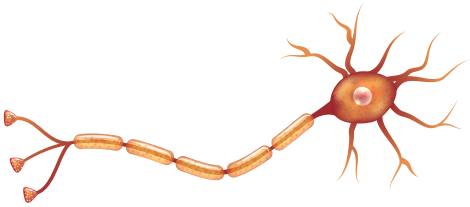
the price Zolgensma would be cost-effective at, according to Novartis.

Novartis is looking at innovative pricing structures for **Zolgensma**, such as installments.

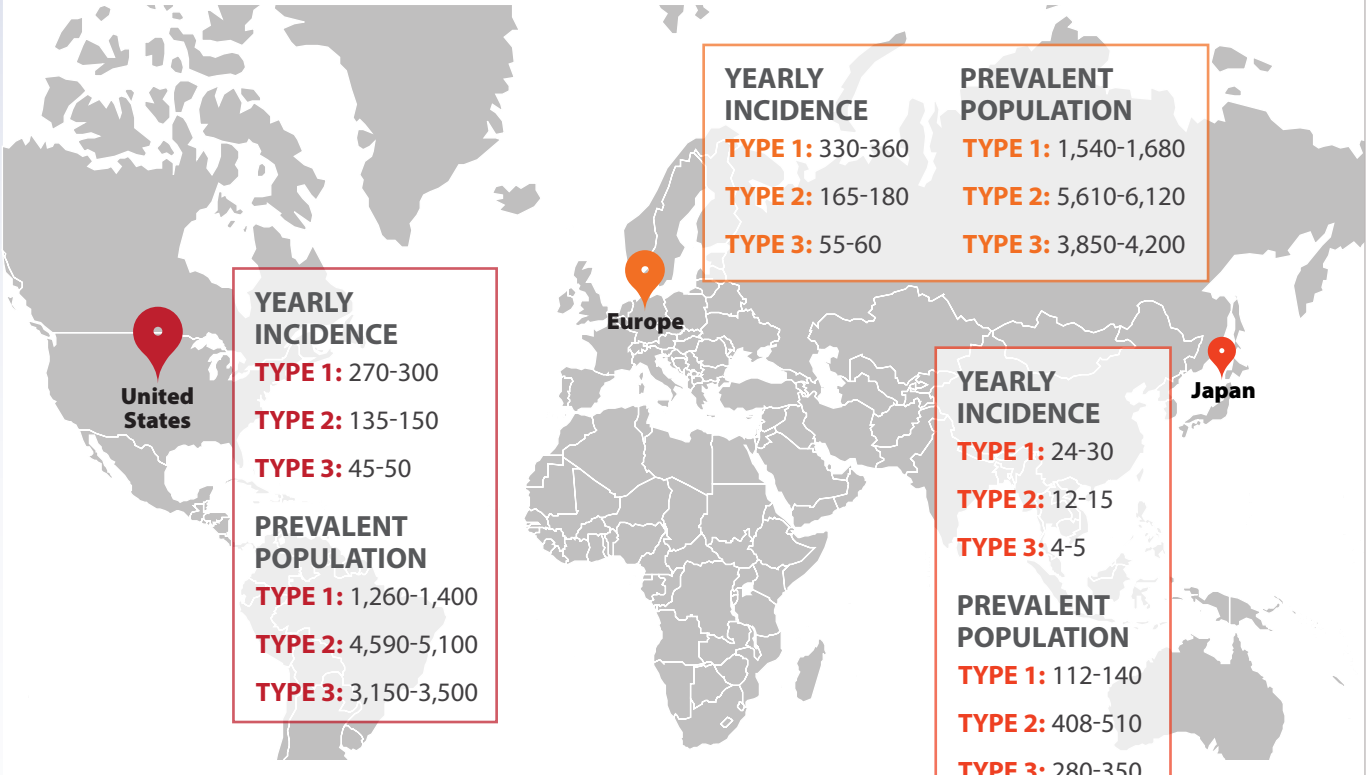
ICER says Zolgensma would be cost-effective at $1.6m, and at $2m it would be more cost-effective than Spinraza.

DISEASE SEGMENTATION

	Age of Onset	Incidence Split/ Prevalence Split[6]	Survival
TYPE 1	<6 months	60% / 14%	95% have life expectancy <18 months
TYPE 2	6-18 months	30% / 51%	68% alive at age 25
TYPE 3	Early childhood to early adulthood	10% / 35%	Normal survival



SMA PATIENTS IN KEY GEOGRAPHIES[6]



Source: [1]SMA Foundation, SMA Support UK, SMA Europe; [2]Biogen earnings conference call, Jan. 29, 2019, https://bit.ly/2tCJCus; [3]Interview with Scrip, Jan. 30, 2019, https://bit.ly/2GKXZFT; [4]Roche results meeting, London, Jan. 31, 2019, https://bit.ly/2Tdt6zH; [5]Pharmaprojects Feb. 5, 2019, Biomedtracker Feb. 11, 2019, SMA Europe, SMA Foundation (US); [6]Novartis R&D and investor update, Nov. 5, 2018, SMA Europe

AbbVie Validates Voyager's One-Shot Approach With Parkinson's Collaboration

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Voyager Therapeutics Inc. has received another important validation for its CNS gene therapy approach by signing a collaboration with existing partner **AbbVie Inc.** on Feb. 22 that will see the pair develop and commercialize "vectorized antibodies" for Parkinson's disease and other diseases characterized by the abnormal accumulation of misfolded alpha-synuclein protein.

Several analysts are encouraged by this deal, with BTIG stating that it could lead to the "first true disease-modifying therapy for PD." Voyager will receive an upfront cash payment of $65m, and has the potential to earn up to $245m in preclinical and Phase I option payments. The gene therapy company is also eligible to receive up to $728m in development and regulatory milestones for each alpha-synuclein vectorized antibody compound. It will also be eligible to receive tiered royalties on the global commercial net sales of each alpha-synuclein vectorized antibody and may earn up to $500m in commercial milestones.

This is the second collaboration in as many months for Voyager, which inked a $65m deal with San Diego-based **Neurocrine Biosciences Inc.** in January to develop gene therapies for Parkinson's and Friedreich's ataxia, along with two future programs.

With these two deals so close together, it is thought by some industry observers that Voyager will now expand the applicability of its adeno-associated vector (AAV) gene therapy technology. "We like this overall direction as getting mAbs into the CNS opens a vast new area of therapeutic space," stated BTIG analysts in an industry note. But they then tempered their enthusiasm by stating that they expected development in this field to be slow moving as the one-time dosing and "constitutive expression of therapeutics may not make sense in all indications."

VOYAGER'S APPROACH

The pharma industry's major challenge in developing therapies for neurodegenerative disease that require frequent doses of large amounts of antibodies has been their delivery across the blood-brain barrier (BBB). Voyager's approach is to deliver a hopefully one-time intravenous dose of the genes that encode for the production of therapeutic antibodies using its blood-brain barrier penetrant adeno-associated virus (AAV) capsids. This approach could result in the potential for higher levels of therapeutic antibodies in the brain compared with current systemic administration of antibodies.

Despite the latest AbbVie link up being so early in development, Morgan Stanley analysts said that they were "optimistic" of Voyager's one-dose strategy to produce greater quantities of antibodies, saying that they "remain encouraged by recent partnerships as they help further validate Voyager's approach and payments from partners offer the opportunity for Voyager to further develop wholly owned product candidates."

There are other candidates further along in the clinical that are also targeting alpha-synuclein in Parkinson's disease patients. **Biogen Inc.** is evaluating BIIB054 in Phase II clinical studies, in a collaboration with **Neurimmune Holdings AG**; and **Roche** and collaborator **Prothena Corp. PLC** are testing PRX002, an alpha-synuclein targeting MAb, in a Phase II study under a 2013 collaboration. Phase II data from these trials are expected in the first half of 2021 and early 2020, respectively.

Last year **Lundbeck Inc.** swerved its usual R&D strategy and entered the clinic with its inaugural monoclonal antibody, Lu AF82422, developed in a collaboration with **Genmab AS** that was set up in 2010. *(Also see "Lundbeck Breaks Into MAb Development, Adds To Suite Of Parkinson's Candidates" - Scrip, 7 Aug, 2018.)*

EXISTING PARTNERS

Little over a year ago AbbVie and Voyager announced their first collaboration, a $69m deal to create an Alzheimer's disease program using a single-administration gene therapy delivering a monoclonal antibody targeting tau protein into the patient's CNS via a targeting mechanism using its AAV technology.

Wedbush analysts said that this latest AbbVie deal suggested "favorable preclinical progress for the tau program, and further validation for Voyager's vectorized antibody approach."

In practical terms, under this latest collaboration Voyager will perform research and preclinical development work to vectorize antibodies directed against alpha-synuclein that are designated by AbbVie. After that AbbVie may select one or more vectorized antibodies to advance into IND-enabling studies and clinical development.

Voyager will be responsible for the research, IND-enabling and Phase I clinical activities and costs. Following completion of Phase I clinical development, AbbVie has an option to license the vectorized alpha-synuclein antibody program for further clinical development and global commercialization for indications including Parkinson's disease – a market which is forecast by *Datamonitor Healthcare* to be worth up to $6.7bn by 2025 – and other synucleinopathies.

ONE EYE ON HUNTINGTON'S

BTIG analysts believe that Voyager's AAV technology could have an impact in Huntington's disease and genetic amyotrophic lateral sclerosis, the latter of which is currently unpartnered, saying that they expect the programs for these two diseases will become "increasingly important" as clinical trials start this year.

Data release in October 2018 from large animal studies showed that a single delivery of Voyager's Huntington's disease clinical candidate VY-HTT01 achieved significant reduction of *HTT* gene expression in deeper tissues and outer layers of the brain. Its genetic ALS candidate, VY-SOD102, achieved a significant reduction of *SOD1* gene expression throughout the spinal cord, including almost complete reduction in cervical motor neurons.

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Sun On Course To Launch Safinamide For Parkinson's In India

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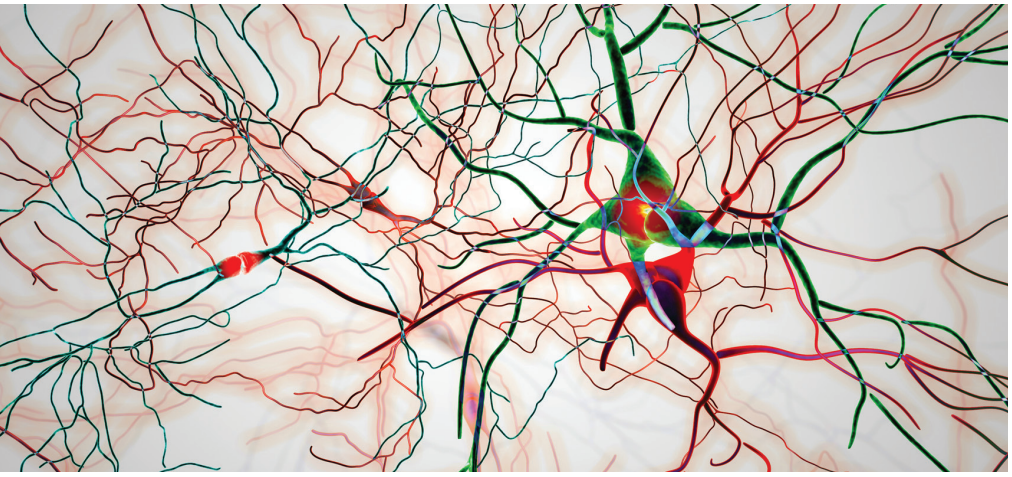
India's top-ranked drug firm, **Sun Pharmaceutical Industries Ltd.**, appears to have inched closer to a potential launch of the Parkinson's disease treatment, safinamide, on the Indian market, after its plans were recently endorsed by a key expert panel that advises the regulator.

Safinamide was discovered and developed by the Bresso, Milan-headquartered **Newron Pharmaceuticals SPA**, which has sewn up a number of alliances to commercialize the product in various markets, although Sun declined to clarify if it had a tie-up with the innovator firm for the product.



It's not immediately clear if Newron holds a valid patent in India for safinamide, although some analysts told *Scrip* that the generally "conservative" Sun, currently firefighting corporate governance concerns, already has enough on its plate and is unlikely to engage in any high-risk launch activity. Newron did not immediately respond to an email request for comment on Sun's emerging plans for safinamide in India.

Safinamide (marketed as *Xadago*) is commercialized by Newron's partner **Zambon Co. SPA**. US WorldMeds holds commercialization rights to the product in the US, while Meiji Seika has the rights to develop and commercialize the compound in Japan and other key Asian territories. In 2017, Meiji and **Eisai Co. Ltd.** firmed up a license agreement under which Eisai received exclusive rights to market safinamide in Japan, as well as to develop and market the therapy in certain Asian markets - India did not feature on the list at the time . *(Also see "Newron Seeks New Assets To Grow Pipeline" - Scrip, 26 Sep, 2017.)*

At the time of its 2017 launch Xadago once-daily therapy had a US list price ranging from $600-700 for a 30-day supply of the 50 mg or 100 mg tablet, roughly in line with **Teva Pharmaceutical Industries Ltd.**'s *Azilect* (rasagiline). *(Also see "Newron's Parkinson's Disease Drug Xadago Priced At $600-700/Month" - Scrip, 23 Mar, 2017.)*

It will be interesting to see how Sun, which is a leader in niche therapy areas such as neurology, psychiatry and cardiology in India, prices safinamide, especially with an eye on access to treatment. Some estimates put the current prevalence of Parkinson's disease in India at around 300-400 in a population of 100,000, which is expected to more than double by 2030.

INDIAN PATIENTS IN GLOBAL STUDIES

Sun's clearance for safinamide appears buttressed by study data from the innovator product, with the subject expert committee (SEC) in India noting that the drug is already approved in the US, UK, EU, Canada and Australia.

Safinamide was approved by the US FDA in 2017 as an add-on treatment for patients with Parkinson's disease who are currently taking levodopa/carbidopa and experiencing "off" episodes. Such episodes refer to a time when a patient's medications are not working well, escalating Parkinson's symptoms, such as tremor and difficulty walking.

The SEC (neurology and psychiatry) observed that in "two global clinical trials (study 016 and study 018), the results of which are already published, majority of the patients were from India" and the study had demonstrated the benefits of safinamide 50mg and 100mg tablets as add-on therapy to L-Dopa and other dopaminergic treatments in mid- to late-stage idiopathic Parkinson's disease patients with motor fluctuations. Both study 016 and study 018 are randomized controlled trials pertaining to safinamide; study 018 was an 18-month extension of study 016.

"After detailed deliberation, the committee recommended for grant of permission to manufacture and market safinamide 50mg/100mg tablets. The product should be sold by retail on the prescription of neurologists/geriatricians," the SEC said at its meeting earlier this month.

Sun did not respond to specific queries on its approval for safinamide by the SEC in India including on aspects related to trial data but told *Scrip* that it was "awaiting" the approval of the Drugs Controller General of India for manufacturing and marketing safinamide in India.

In general, under India's tweaked review process, a go-ahead from the SEC for new drugs and global clinical trial proposals usually means that no further approval of the Technical Committee or Apex Committee is typically required, though reviews are possible in certain circumstances. The previous three-layered system required SEC recommendations to be vetted by the Technical Review Committee and then cleared by the Apex Committee.

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Bayer Confident It Can Cope With Patent Cliff Pain

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While **Bayer AG** admits that there is work to be done in restocking its pipeline, the company's management is confident that the loss of patent protection on its two biggest-selling drugs – Xarelto and Eylea – can be overcome with the help of at least some of the 50 projects currently in clinical development.

The importance of the anticoagulant *Xarelto* (rivaroxaban) and eye drug *Eylea* (aflibercept) was further highlighted at the German group's annual press conference in Leverkusen on Feb. 27. For the fourth quarter of 2018, pharmaceutical sales were up 1.8% to €4.29bn, and Xarelto made up €993m (+8.6%) of that; Eylea contributed €600m, up 18.3% on the year-earlier period and analysts have regularly expressed concern about Bayer's reliance on the two blockbusters. *(Also see "Q4 Preview: How Will Bayer Survive Patent Cliff?" - Scrip, 13 Feb, 2019.)*

However, speaking to *Scrip* at the Leverkusen meeting, head of pharma Stefan Oelrich said that the pipeline looked in reasonable shape and noted that the much-mentioned patent cliff is not exactly imminent as it will probably not be until 2024 or 2025 that Bayer suffers significant drops in revenue. He added that Xarelto (teamed with **Johnson & Johnson**) and Eylea (with **Regeneron Pharmaceuticals Inc.**) proved that "we have a very good track record in partnering, we are known in the industry for this," and he expected more such deals to come as the company increases its efforts on external collaborations.

Chairman Werner Baumann backs pipeline promise

Bayer chairman Werner Baumann spoke about one such alliance, the one forged with Finland's **Orion Pharma**, for darolutamide, an oral treatment for prostate cancer. Last year saw the

successful conclusion of a Phase III study which showed that the drug significantly extended metastasis-free survival and Bayer announced that it had completed a rolling marketing application in the US. *(Also see "Bayer Sees Room For Third-To-Market Darolutamide In Prostate Cancer" - Scrip, 14 Feb, 2019.)*

This sets up a possible approval later this year and Baumann said the firm estimated the peak sales potential of darolutamide to be at least €1bn. He had the same sales forecast for finerenone, which is currently in Phase III for the treatment of patients with diabetic kidney disease.

As for *Vitrakvi* (larotrectinib), the sales forecast for the tissue-agnostic drug for which Bayer has recently assumed sole responsibility from ex-partner **Loxo Oncology Inc.** (which has just been acquired by **Eli Lilly & Co.** for $8bn), is over €750m. Vitrakvi was approved by the FDA last year, and launched in November, for locally advanced or metastatic solid tumors with a neurotrophic tyrosine receptor kinase (NTRK) gene fusion.

Oelrich told *Scrip,* "I can't give you the exact number of patients that we have on it but as it is a very specialized medicine, we're tracking actually each and every one that's on treatment right now. Anecdotally I can tell you that doctors are saying that when the patient responds, the cancer is melting away. It's an amazing thing and it works across all tumor types."

He acknowledged that finding the patients who would benefit from Vitrakvi remained a big challenge, given there are expected to be only around 2,500 to 3,000 new cases per year in the US and testing for the mutation is not yet common. However, given that genomic data analysis and diagnosis is becoming more affordable, "I think we're going to see increased testing especially in pediatrics," Oelrich added, "We had a patient in Italy that was diagnosed with the NTRK fusion in the womb so potentially an unborn child is getting treatment now that anomaly is going to be fixed, so to speak."

Oelrich went on to say how he spoke to a colleague from another company this week about "how we as an industry who are advancing precision medicine have to maybe come together and see how we can actually do testing as more of a joint effort. At the moment, it's a a little bit looking for a needle in the haystack which is why the uptake of this type of therapy is going to be slow but the beauty of Vitrakvi is that once you have identified a patient and if you're not too late, and if that tumor melts away, as has been anecdotally reported, these patients will take that therapy for a long, long time." *(Also see "French Patients To Get Pre-Approval Access To Bayer's Vitravki" - Pink Sheet, 20 Feb, 2019.)*

Back to the patent cliff, he said that there was still plenty of life in Xarelto, pointing to the additional indication of coronary or peripheral arterial disease (CAD/PAD) for which the drug was approved in the US in October. *(Also see "Keeping Track: Xarelto Earns CV Risk Reduction Claim In Quiet Week; Spotlight On Formal Dispute Resolution" - Pink Sheet, 14 Oct, 2018.)*

Oelrich claimed that the latter represented a great opportunity and moved Xarelto from pure anticoagulation into a new set of patients. CAD/PAD represents "an incredible unmet need" and "we need to educate physicians out there that now you have a new therapeutic option that will extend patients' lives in an unprecedented way in this cardiological setting where before that, physicians not in their deepest thoughts or dreams would have considered an anticoagulant for those patients, that was a no go. Now, the evidence is there that you should because otherwise you will take away life from those patients."

He added: "We need to explain this so there is an investment needed and it's significant and on top of that, we need to compete with our friends that sell new oral anticoagulants (NOACs)," such as **Boehringer Ingelheim GMBH**'s *Pradaxa* (dabigatran), **Pfizer Inc.** and **Bristol-Myers Squibb Co.**'s *Eliquis* (edoxaban) and **Daiichi Sankyo Co. Ltd.**'s *Savaysa/Lixiana* (apixaban) that do not have as many approved indications. "We need to make sure that they don't eat us for breakfast because we do all the education and they take all the sales so probably we need to be investing more," Oelrich added.

There was some concern about the performance in the fourth quarter of another established big earner, notably the prostate cancer radiopharmaceutical *Xofigo* (radium 223). Fourth quarter sales were down 20% to €81m, which Oelrich said was an effect of the early termination of the Phase III ERA223 study combining the drug with J&J's *Zytiga* (abiraterone) due to an imbalance in deaths in patients treated with Xofigo. However, he said that Bayer was still sticking with its €1bn peak Xofigo sales forecast. *(Also see "Bayer Shrugs Off Xofigo Sales Pressure From Study Halt" - Scrip, 1 Dec, 2017.)*

When asked about strategy in terms of acquisitions or licensing products, he said that "personally, I prefer to go as early as possible because otherwise you're taking shortcuts and shortcuts cost a lot of money." Oelrich cited the 'Leaps by Bayer' model which operates from locations in Berlin, Boston and San Francisco and has so far invested some €600m in start-ups and collaborations.

Those investments, which have been made over the last three or four years, "are already starting to pay off," he said, "and we are seeing amazing advances being made and we already hold licensing rights to some of those…and we also have, in some cases, the possibility to take over the entire company." Oelrich argued that "when your innovation is not good you either buy something or you do the basic footwork and so far we've been extremely successful at doing this…we have a fantastic track record of developing medicines in this company."

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Mylan Spooks Investors With Surprise Plans For Higher 2019 Spending

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Investors hate uncertainty, a fact underscored when **Mylan NV**'s management during its fourth-quarter update said 2019 would see a big jump in R&D spending and higher selling, general and Aaministrative (SG&A) expenses, but left key questions unanswered about the drug makers' future portfolio, triggering a sell off in the group's shares.

Mylan's stock price was also weighed down by news the generic and specialty drug maker expected 2019 revenues to range between $11.5-12.5bn, which is essentially flat with 2017, and that 2019 adjusted earnings were expected to be between $3.80 to $4.80 per share, significantly below the $5.02 average of Wall Street estimates – and down both year-on-year and around the levels of 2016.

The company's update, made on Feb. 26, prompted many analysts to adjust downwards their projections for Mylan.

ANALYST REACTION

Analysts at Cowen were decidedly bearish, noting that the company's retrenchment moves come "despite a tremendous amount of company and product acquisitions."

"Despite the roughly $15bn spent, and over $2bn in EBITDA purchased, this business is generating no additional cash than in 2015. And even with the approvals and launches of *Copaxone*, *Neulasta* and *Advair*, these approvals are only providing some relief – but are not altering the systemic problems inherent with the generic model," analysts at Cowen said in a note to investors.

A more sanguine tone came from BMO, which said that while Mylan "surprised investors with its level of SG&A spend going forward, driving an EPS range below expectations, we don't disagree with Mylan's strategy to meaningfully step-up investments behind key products if it will drive greater top-line growth … But it will likely take time to demonstrate that execution."

STRATEGIC REVIEW NEARING COMPLETION

The Morgantown, WV-based company has been steadily trimming its forecasts as it navigates a volatile generic-drug market. Falling prices for copy-cat medicines in the US prompted Mylan last year to start reviewing strategic options, such as a structural revamp. Its chief executive officer Heather Bresch told an analysts call that Mylan was close to completing that strategic review, and that the drug maker would do "everything and anything" to unlock value as sales decline.

MORGANTOWN PLANT

Another dark cloud is the continuing problems at a Mylan plant in Morgantown. Management indicated it continued to address the issues related to a regulatory warning letter received in late 2018. The plant continues to supply products, but no significant new product revenue from there is forecast in 2019. Mylan received a warning for its Morgantown site in November.

Still, Mylan's management sounded upbeat throughout the update, and voiced confidence in its ability to benefit from anticipated growth of complex, specialty and biologics products.

CEO Bresch said, "Through leveraging the diversification across our commercial, operational and scientific platforms, we feel incredibly positive about our ability to deliver a strong top-line financial performance in 2019."

President Rajiv Malik added that Mylan anticipated "growth of more than $1bn in new launches, nearly all of which have already been approved, and which reflects a heavier weighting on specialty and complex generic products aligned with the evolution of the pharmaceutical industry."

He added, "Given the evolution of the US market and dynamics of the commodity generics, we also continue to evaluate our R&D program and resource allocation, and from here onwards, we'll further increase the emphasis on moving up the value chain with a focus on complex, specialty and biologics opportunities, the NCE and brand life cycle management strategies."

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UK Offers Pharma Firms Ferry Tickets To Avoid No-Deal Brexit Supply Disruptions

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The UK government has produced its most detailed account yet of the steps that are being taken to mitigate the effects of a no-deal Brexit on the supply of medicines, vaccines and other medical products, including the offer of ferry tickets "at market rates" to pharmaceutical companies wanting to transport products via alternative shipping routes between EU and UK ports.

To "help ensure the continuation of medicines and medical supplies in the event of a no deal exit," the government has also arranged buffer stocks, stockpiling and additional warehousing space, as well as implementing regulatory changes, health minister Stephen Hammond said in a written statement to parliament.

The "vast majority" of pharmaceutical companies have confirmed that they have stockpiling plans in place, while companies with

products that cannot be stockpiled, such as radioisotopes, have been asked to look at alternative supply routes, the minister said.

His statement came shortly before the government published a paper on the implications of a no-deal Brexit on business and trade in general, in which it says that the flow of goods through the UK Channel port of Dover would be "very significantly reduced for months." The paper states that despite warnings from the government, "there is little evidence that businesses are preparing in earnest for a no deal scenario, and evidence indicates that readiness of small and medium-sized enterprises in particular is low."

A no-deal Brexit still remains a possibility, although the likelihood of this happening may have shrunk after the prime minister, Theresa May, shifted her position and declared on Feb. 26 that she would allow the parliament to vote on whether to allow such a scenario or to delay Brexit for a short period if it did not agree to her Brexit deal in a vote to be held on March 12.

The government has already issued numerous "technical notices" about the possible impacts of a no-deal Brexit, and what actions the government has taken, and businesses need to take, to mitigate them. In the life sciences area, these include buying up additional warehousing space to accommodate the additional six weeks' worth of medicines stockpiles that pharmaceutical companies have been asked to build up.

In his Feb. 25 statement, Hammond gave more details of the concrete steps that have been taken to date. Reiterating earlier warnings that all players, including pharma firms, need to pull their weight to palliate the more serious effects of a no-deal, Hammond said: "While we never give guarantees, we are confident that, if everyone – including suppliers, freight companies, international partners and the health and care system – does what they need to do, the supply of medicines and medical products should be uninterrupted in the event of exiting the EU without a deal."

BUILDING BUFFER STOCKS

Working with the pharmaceutical and medical device industries as well as the healthcare system, he said, the Department of Health and Social Care has analyzed the supply chains for 12,300 licensed medicines, "close to half a million product lines of medical devices and clinical consumables, vaccines used in national and local programmes, and essential non-clinical goods on which the health and care system relies, such as linen, scrubs and food."

Of the 12,300 products that the department has analyzed, about 1,800 are no longer marketed in the UK. As for the 7,000-odd prescription-only and pharmacy-only medicines "with an EU/EEA touchpoint" that are on the market, the department has been working with suppliers to ensure they increase their buffer stocks to hold at least an additional six weeks of stock before March 29, when the UK is due to leave the EU, Hammond said.

"The vast majority of companies have confirmed stockpiling plans are in place. For those medicines that cannot be stockpiled because, for example, they have short shelf-lives, such as medical radioisotopes, we have asked suppliers to make alternative routes using airfreight, which some suppliers already do now." 500 "general sales list" medicines (those that can be bought over the counter) have an "EU touchpoint" and the government is working with suppliers to "assure contingency plans for those products." Similar measures are being applied for the supply of vaccines in terms of stockpiling and warehousing, with Public Health England working with vaccines suppliers to ensure replenishment of existing stockpiles "in the event of supply disruption in the UK," Hammond said. His department is also working with organizations running clinical trials, and has asked them to "ensure contingency arrangements are in place for their supplies. Supplies of clinical trials are transported in small quantities and usually via airfreight."

WAREHOUSING AND FREIGHT ARRANGEMENTS

The DHSC has agreed contracts on additional warehouse space to store stockpiled products, including ambient, refrigerated and controlled drug storage. "Last week we updated industry on how they can access this additional storage," Hammond declared.

As for avoiding potential blockages in the normal shipping routes via Dover in the southeast of the UK, the government has secured additional Roll-on, Roll-off (RoRo) ferry capacity as of March 29.

Hammond said the Department of Transport had signed contracts with two ferry companies for the next six months, using routes away from the Dover Straits, where most goods arrive by sea from the EU. These alternative routes are Cherbourg-Poole, Le Havre-Portsmouth, Roscoff-Plymouth, Caen-Portsmouth, Vlaardingen-Immingham, Cuxhaven-Immingham and Vlaardingen-Felixstowe.

The government has already purchased the tickets from the shipping freight operators, and "these will be sold on at market rate," Hammond said. "There is cross Government agreement that all medicines and medical products will be prioritised on these alternative routes to ensure the flow of all these products may continue unimpeded."

Companies that supply medicines or medical goods "will be offered the option of buying tickets on these routes and my Department is currently engaging with industry to ascertain the likely uptake levels," he continued. "We have worked with the pharmaceutical industry to ensure that planes are contracted to bring in medical radioisotopes under the appropriate specialist conditions."

The UK BioIndustry Association said the government had written to marketing authorization holders outlining operational details about shipping routes between the EU and the UK and on the warehousing capacity for additional buffer stock, and asking them to register and complete a survey. In a Feb. 26 blog, it said that the registration and survey would "provide volume requirements for the transport contingency requirements, and be the way by which companies will be able to book ferry tickets for the government chartered ferry capacity in the event of no-deal. It is vital that BIA members submit their responses TODAY." It advised companies that had not yet received the letter to contact the DHSC.

REGULATORY ASPECTS

A "multi-layered approach is essential" to dealing with the likely effects of a no-deal Brexit, including regulatory preparations, Hammond said. Alongside the practical measures to protect supply chains, the UK regulatory body, the MHRA, has issued several guidance documents and regulations on what would happen to drug regulation if the UK left the EU without a deal.

These cover key areas such as new drug approvals procedures, "grandfathering" of existing EU marketing authorizations and pediatric and orphan exclusivities.

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Building A Biotech: Industry Veteran Moroney Reflects

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"I would never have imagined at the outset that we could have been so productive." - Simon Moroney, CEO of MorphoSys

Simon Moroney, co-founder and CEO of Munich-based biotech **MorphoSys AG** has made clear his plans to retire by June 2020. He has been at the helm of MorphoSys since its inception 27 years ago, and believes that the company has now reached a turning point, becoming more competitive and controlling its own destiny, which creates an opportune point to hand the reins to someone that can lead the company through its next stage of development.

In an exclusive interview with *Scrip*, New Zealand-born Moroney said he felt it was vital to ensure the company was in great shape before he took the decision to leave. "It's in a really strong position; its prospects have never been better. So it feels totally like the right time for me and for the company: from that perspective I feel very good about it."

The past three years have seen the biotech make moves that will catalyze the next stage of its growth. MorphoSys licensee **Janssen Biotech Inc.** gained approval in the US and Europe for the plaque psoriasis drug *Tremfya* (guselkumab), to which MorphoSys will be entitled to royalties; it filed an IPO on the NASDAQ to garner US investment; and it received FDA breakthrough therapy designation for MOR208, its proprietary lymphoma antibody for relapsed or refractory diffuse large B cell lymphoma.

After years of partnering with big pharma such as **Roche** and **Novartis AG**, MorphoSys is to commercialize MOR208 itself, potentially from the middle of 2020. This, coupled with the appointment of David Trexler, ex SVP of **EMD Serono Inc.**'s US oncology commercial division, as the new president of the company's recently founded US subsidiary, MorphoSys US Inc., show a company gearing up to be commercially more assertive.

"We'd be in the market, up against much bigger companies than us, much more experienced commercial companies, so we understand the magnitude of that challenge," said Moroney. "We think we're up for it. There are multiple examples of American companies, mainly, that have done this themselves, so we're not trying to do anything totally new here, but it will be a new step in the company's development, there's no question. We're preparing for it very actively."

There will be a rolling submission during the course of this year to the FDA for MOR208, which will complete by the end of 2019. MorphoSys is hoping for approval by around mid-2020.

Moroney will remain a shareholder and says he is "super excited about what's coming along," but concedes that he doesn't need to be CEO for the next stage of the company's evolution.

While the commercialization of MOR208 will potentially coincide with his departure, Moroney will retain a strong vested interest in the success of the drug, and the rest of the blossoming pipeline. The company currently has more than 100 programs in total, with 29 of those in clinical development.

"I'm not aware of any other single platform in the industry that has been so productive," said Moroney. "We're talking here about a single platform. It helps that we're in an area – antibodies – which can be widely applied across multiple indications. I would never have imagined at the outset that we could have been so productive."

A BURGEONING CONCERN

The outset that Moroney refers back to was in 1992. He had been working in academic positions at institutions including Cambridge University and Harvard Medical School but had had a taste of industry with a stint at **ImmunoGen Inc.** working on the first generation of anticancer antibody conjugates.

Having realized that publishing and teaching did not hold his interest as they once had, and with the "challenge of building something significant" turning his head, Moroney and his colleague Christian Schneider formed the idea to build a platform technology company.

The pair then approached Andreas Plückthun, an antibody engineer who had made several important breakthroughs in the field. With Plückthun on board, and his technology forming the nucleus of the company, MorphoSys started out with €150,000 in venture capital funding and a pretty big challenge; to build a collection of over one billion different human antibodies as a basis for the development of new drugs.

"We started it as an absolutely trainee start-up with nothing and almost no money and so developing our own drugs to any extent was just not realistic at that time," said Moroney. In the early 1990s, the platform technology business model was en vogue, he recalled. "At the time, it was frowned upon to try and develop drugs yourself. That sort of heritage is visible in our incredibly broad pipeline, which is so broad because we worked with so many different pharmaceutical companies in the early days." Today, the company's partnership roster is an A-Z of the pharmaceutical industry. Names such as **Pfizer Inc.**,

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Scrip's weekly **Pipeline Watch** tabulates the most recently reported late-stage clinical trial and regulatory developments from the more than 10,000 drug candidates currently under active research worldwide.

Click here for the entire pipeline with added commentary: http://bit.ly/2mx4jY3

PIPELINE WATCH, 22–28 FEBRUARY 2019

Event Type	Lead Company/Partner	Drug Name	Indication	Trial And Outcome	Change To LOA (%)	LOA (%)
Phase III Published Results	DBV Technologies	Viaskin Peanut	Food Allergies	PEPITES; JAMA, Feb. 22, 2019	0	60
Phase III Published Results	Catalyst Pharmaceuticals Inc.	Firdapse (amifampridine)	Lambert-Eaton Myasthenic Syndrome	Journal of Clinical Neuromuscular Disease, Feb. 26, 2019	0	100
Phase III Updated Results	Actinium Pharmaceuticals, Inc.	Iomab-B	Bone Marrow Transplant	SIERRA; Encouraging Results	0	37
Phase III Updated Results	Regeneron/Sanofi	Dupixent (dupilumab)	Chronic Rhinosinusitis With Nasal Polyps	SINUS-52 (w/ MFNS); Positive Results	0	71
Phase II/III Updated Results	Swedish Orphan Biovitrum/Novimmune SA	emapalumab-izsg	Hemophagocytic Lymphohistiocytosis	04 (Paediatric); Encouraging Results	0	100
Phase II/III Updated Results	BeyondSpring Pharmaceuticals, Inc.	plinabulin	Neutropenia/Leukopenia	Protective-2 (China); Improved Efficacy	0	60
Phase III Top-Line Results	Novavax, Inc.	ResVax (RSV vaccine)	RSV Infection	Prepare; Mixed Results	0	55
Phase III Top-Line Results	Horizon Pharma plc	teprotumumab	Thyroid Eye Disease	OPTIC; Met Primary Endpoint	0	51
Phase III Top-Line Results	AstraZeneca PLC	Brilinta (ticagrelor)	Coronary Artery Disease And Diabetes	THEMIS; Met Primary CV Events Endpoint	5	52
Phase III Top-Line Results	Santhera Pharmaceuticals	Catena (idebenone)	Duchenne Muscular Dystrophy	SYROS; Slowed Respiratory Function Loss	3	64
Phase III Top-Line Results	AstraZeneca/Merck & Co	Lynparza (olaparib)	Pancreatic Cancer, First-Line Maintenance	POLO; Improved PFS	10	45
Phase III Top-Line Results	Johnson & Johnson/Morphosys	Tremfya (guselkumab)	Psoriasis	ORION (Self- Dose Device); Safe And Effective	0	100
Phase III Top-Line Results	Foamix Pharmaceuticals Ltd.	FMX103 (minocycline) topical foam	Rosacea	FX2016-13 (Long-Term Safety); Favorable Profile	3	73

Source: Biomedtracker | Informa, 2019

CONTINUED FROM PAGE 21

Merck KGAA, **GlaxoSmithKline PLC** and **Bayer AG** all make an appearance, using MorphoSys proprietary platforms HuCAL and Ylanthia to discover and develop antibodies.

In the past 27 years the company has changed organically. Essentially starting out as a services business it transformed into a development business which required a big change within the company, both in culture, personnel and in-house expertise, see timeline below. "Now we're standing at the beginning of the next change," said Moroney, adding that the company's focus is on its proprietary programs.

With the long-standing CEO's departure the biggest shift in the company's evolution to date, and by treading in commercialization territory, it will have to toughen its shell to the highs and lows of a globally competitive industry.

RECENT SETBACKS

A fresh example is the January US court ruling against MorphoSys in its three-year patent dispute with Danish biotech **Genmab AS** and pharma giant **Johnson & Johnson** over *Darzalex* (daratumumab). Moroney appears surprisingly relaxed when he comments on the patent decision. "Of course we invested in the protection of our IP, but in the end, a court case case is always a bit like a lottery ticket."

"It was disappointing, obviously. We would have love to have prevailed; we would love to have a royalty on Darzalex. But it wasn't to be and honestly, it doesn't really matter for us. We still have patent protection on MOR202, which is the key protection we need."

In the ruling three US patents were ruled invalid, those patents were only important to MorphoSys in that they may have covered Darzalex and therefore, earned the German biotech a royalty on the blood cancer blockbuster. Moroney said the company was "caught out a little bit" by a "real tectonic shift in the way patent law is interpreted in the US," which will affect other companies. "That was something that we couldn't have expected at the time that we launched the suit and it just turned out that way; it's unfortunate," he said.

ONWARDS AND UPWARDS

Moroney is undecided in his next move. He feels he could be helpful as an advisor to European biotechs, but has no solid plans, and will not be starting a new company.

Through his 27 years in the European biotech community Moroney has witnessed many a biotech boom and bust. The lack of ambition and belief within smaller European biotechs is sometimes a worry, he said, and he hopes that MorphoSys can inspire smaller companies to be competitive on a global scale. "I hope that MorphoSys has acted as a kind of beacon, a lighthouse if you like, of what other European biotech companies can be like."

Moroney's message to inspire small European companies is to be confident: "You don't have to give your product away early; you can go out and raise sizable amounts of money to do the development yourself, to hang onto the rights yourself."

He regrets that there aren't more large European biotechs, but cites the success of companies such as **Galapagos NV**, Genmab and **Evotec AG** as examples to smaller companies to develop drugs themselves, which "is the real way of creating value in this industry."

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APPOINTMENTS

Executive	To Company	New Role	From Company	Previous Role	Effective Date
Herb Cross	Atreca Inc	Chief Financial Officer	ARMO BioSciences	Chief Financial Officer	25-Feb-19
Hardean E. Achneck	Dicerna Pharmaceuticals Inc	Vice President and Head, Medical Development	Sanofi Genzyme	Head, Partner Relations and Global Business Development	21-Feb-19
Athanasios Papadopoulos	Emergex Vaccines Ltd	Chief Medical Officer	Sanofi	Vice President, Senior Director	1-Mar-19
Christopher Moxham	Fulcrum Therapeutics	Senior Vice President, Discovery	Eli Lilly & Co	Vice President, Quantitative Biology	20-Feb-19
Kenneth Huttner	LogicBio Therapeutics	Senior Vice President, Head, Clinical Development	Bioverativ	Vice President, Clinical Development	22-Feb-19
James J. Ferguson	Matinas BioPharma Holdings Inc	Chief Medical Officer	Amgen	Head, US Medical Affairs	25-Feb-19

Click here for all appointments: https://bit.ly/2oHWRYn

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