Scrip
Informa Pharma Intelligence
No. 3974
September 27, 2019

Roche: We've Abandoned Budgets And It's Liberated Employees

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

Big pharma is constantly looking for new ways to control its multi-billion dollar budgets and speed up processes across R&D and commercial divisions. How tightly managers have been able to manage these targets has been a key internal metric.

But what if one of these huge corporations were to abandon that core competency of controlling costs, and simply did away with budgets altogether?

This is exactly the radical approach Roche has taken in its commercial division, and three years in, the company says the business and its employees are reaping the rewards.

Bill Anderson, CEO of Roche's pharma division, says the initiative, which was first introduced in 2016, is boosting productivity and empowering employees.

Speaking at the Roche Pharma Day for investors in London on 16 September, he said: "On the commercial front, we've eliminated budgets in most of the world. And basically, we've replaced that with an understanding of what people are to deliver."

He says budgeting is often "plastic exercises that people went through…almost like a ritual or a game" which has proved counterproductive to team performance.

Freed of this major time commitment, Anderson says commercial teams have been told to focus instead on delivering advances for patients and meeting customer needs.

He says they are expected to be sensible with company resources but otherwise spending and resource use won't be reviewed until the activity is complete.

"We're not going to spend our time planning and budgeting and gaming and micromanaging targets. The answer to everything is 'Go ahead, and we'll talk about how you did later.' And this is having a dramatic effect on the pace. We see progress accelerating all around the world."

PRODUCTIVITY IS UP

He offered up examples of increased productivity, including a 50% increase in the number of molecules at pivotal stage in clinical development over a three-year period.

Spending on product development has risen 12% in the same time, while headcount is up just 4%.

"So, we have essentially the same [number of] people taking care of 50% more molecules," Anderson says. This approach is now being rolled out across divisions.

The US pharmaceutical business was an early adopter of the approach, and has seen sales growth of 40%, set against operating expenses rising just 6% while headcount declined 6%.

It may be too early to draw a direct correlation between this streamlined approach and Roche's new surge in pipeline productivity and commercial success with products such as Ocrevus, Hemlibra and Tecentriq, as there are plenty of other dynamics at play.

However, there is no doubt that it makes for an attractive message in the war for top talent. Big pharma has increasingly seen its star performers lured away to work for leaner and faster biotechs and specialist pharma companies. Making

CONTINUED ON PAGE 4

Going Digital
Sanofi & Bayer pursue platform tech (p10)

First Oral GLP-1
US approval for Novo Nordisk's Rybelsus (p11)

Fujifilm Stem Cell Deal
Licenses Cynata's GvHD asset (p6)

from the editor

eleanor.malone@informa.com

It is intriguing to read of Roche's radical approach to cost management (see cover story). The fact that the initiative has been going for three years and is being expanded speaks to its success.

It's not the first time that the Swiss giant has taken a creative approach to bureaucracy. A decade ago, it ran a controlled experiment to see if transparency could replace pre-approval red tape in travel and expense processes and result in increased staff motivation, process simplification and cost reduction.

The experiment, documented by Roche IT strategist Paul Lambert in a 2011 post on managementexchange.com, changed the process for two groups of employees in Germany in Switzerland, allowing them to make their own decisions, while two control groups in those locations continued to follow the old procedure of gaining manager approval for travel and expenses in advance. The details of the expenses incurred by those in the experimental arm were posted where others could see them, unlike those in the control groups.

The experiment showed that motivation went up and red tape and costs went down in the experimental groups. Lambert is now vice-president commercial IT for Roche Diagnostics, and his bureaucracy-busting philosophy appears to have been catching on more widely across the group.

Because of the necessary tight regulation of medicines development and marketing, pharma is an industry that is particularly beset by red tape. Nevertheless, it is also an industry founded on imagination, experimentation and risk. Roche has shown that harnessing these attributes to battle bureaucracy as well as disease can be very worthwhile.

Scrip
Informa Pharma Intelligence

LEADERSHIP
Phil Jarvis, Mike Ward, Karen Coleman

SUBSCRIPTIONS
Dan Simmons, Shinbo Hidenaga

ADVERTISING
Christopher Keeling

HEAD OF PUBLICATION DESIGN
Gayle Rembold Furbert

DESIGN
Paul Wilkinson

EDITORIAL OFFICE
Blue Fin Building
3rd Floor, 110 Southwark St
London, SE1 0TA

CUSTOMER SERVICES
US Toll-Free: +1 888 670 8900
US Toll: +1 908 547 2200
UK & Europe: +44 (20) 337 73737
Australia: +61 2 8705 6907
Japan: +81 3 6273 4260
Email: clientservices@pharma.informa.com

TO SUBSCRIBE, VISIT
scrip.pharmaintelligence.informa.com

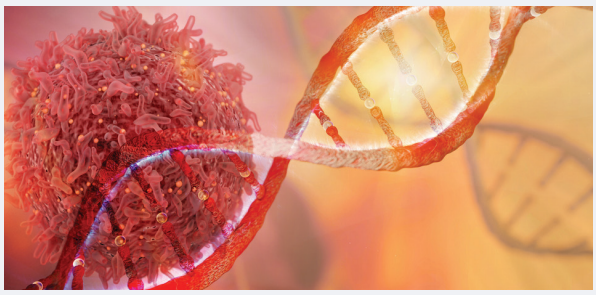
TO ADVERTISE, CONTACT
christopher.keeling@informa.com

All stock images in this publication courtesy of www.shutterstock.com unless otherwise stated

exclusive online content

Boundless Bio Launches With $46m And Novel Oncology Focus On Extrachromosomal DNA

MANDY JACKSON mandy.jackson@informausa.com



Former Ignyta Inc. chief operating officer Zachary Hornby helped the developer of Roche's now-approved tumor-agnostic therapy Rozlytrek (entrectinib) transition its assets to the Swiss big pharma after it was acquired for $1.7bn, then set out to find a new cancer drug development opportunity. Hornby passed on multiple immuno-oncology technologies before settling on the extrachromosomal DNA (ecDNA) work now under way at Boundless Bio, which has raised $46.4m in venture capital.

San Diego-based Boundless emerged from stealth mode on 19 September to announce its series A round, led by ARCH Venture Partners and City Hill Ventures. The company is focused on ecDNA research pioneered by co-founder Paul Mischel at the University of California, San Diego (UCSD) and other scientists who uncovered the link between ecDNA and rapid cancer progression in patients whose tumors have high copy number amplifications of oncogenes.

Mischel is a UCSD School of Medicine professor and a member of the Ludwig Institute for Cancer Research. Other Boundless scientific co-founders include Vineet Bafna, a UCSD professor of computer science and engineering; Howard Chang, a cancer genomics and genetics professor at Stanford University; Ben Cravatt, a chemical biology specialist at The Scripps Research Institute in San Diego; UCSD bioengineering professor Prashant Mali; and Roel Verhaak, professor and computational biology specialist at The Jackson Laboratory's Farmington, CT campus.

Published online 19 September 2019

To read the rest of this story go to: https://bit.ly/2kRHm21

inside:

CONTINUED FROM PAGE 1

work more meaningful and rewarding is now key.

Anderson says the changes have transformed "what it means in terms of the average person at our company's ability to make a difference" for patients.

Also speaking at the London event was Teresa Graham, who took over the role of head of global product strategy in May 2019. "What I see in the halls every day are a lot more people trying to tackle the challenges that matter in the market versus trying to make incremental steps."

She says individuals are more focused on customer and patient needs – something which should also translate into a commercial gain.

"I see a lot more co-creation with customers and health systems where we're actually going out and trying to find proactive solutions to things that we know will hold adoption of our products back for patients. And there's just a very different energy and buzz than there used to be."

EXTERNAL VIEWS

So just how significant is Roche's move?

Mike Rea is the CEO of IDEA Pharma, a strategic consultancy for the sector. He says the plan contains the "kernel of an interesting idea" but points out that greater freedom from budget planning won't directly improve the commercial decision-making which can make or break a product.

> "We're not going to spend our time planning and budgeting and gaming and micromanaging targets. The answer to everything is 'Go ahead, and we'll talk about how you did later.'" – Bill Anderson

"The crucial question is how you add value to what you've got in your pipeline. This sounds like an intriguing approach, but it doesn't automatically translate into better strategic decisions or allocation of resources."

He says this has been demonstrated in immuno-oncology, where Roche (with Tecentriq) has been outmaneuvered by Merck & Co. Inc. and Bristol-Myers Squibb Co. (with Keytruda and Opdivo), though he believes Roche has arrived at a winning strategy for Ocrevus in MS.

"I like the principle of removing internal red tape and admin required with internal cost centre management and budgets," say Stephanie Hall, managing director of brand planning consultancy Uptake Strategies. "Although from a marketing effectiveness perspective it would be hard to define clear ROI, promotional effectiveness, without at least clear tracking of spend on content/channel/customer mixes."

NOVARTIS UNBOSSED

Roche isn't the only company putting its money where its mouth is on cutting internal bureaucracy and empowering its teams.

Its Basel neighbor and rival Novartis AG has introduced an 'Unbossed' culture, whereby managers are seen as accountable to teams, and not the other way round.

However not all big pharma attempts to radically re-imagine working practices have worked.

GlaxoSmithKline PLC famously abolished revenue targets for all global sales teams in 2013 after Chinese authorities punished it for bribery allegations. But earlier this year the company announced that it would be reinstating incentive targets (albeit with a closer eye on ethics) for its front-line reps, having found that it was losing out to rivals in attracting the best sales operatives.

Published online 18 September 2019

Bucking Biosimilar Threat, Roche Sees Further Growth

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

Roche has already enjoyed a vintage 2019, having shrugged off an initial onslaught from biosimilars in Europe thanks to better than expected growth from new products.

Three drugs have been the star performers – multiple sclerosis product Ocrevus (ocrelizumab), immuno-oncology therapy Tecentriq (atezolizumab) and Hemlibra (emicizumab) for hemophilia – and analyst consensus is that each of these could reach sales of $3.5bn or above by 2023.

The Swiss pharma company has also seen two cancer drugs approved this year – Polivy (polatuzumab) for lymphoma and Rozlytrek (entrectinib) in lung cancer.

Roche

In London on 16 September, the company's senior executives expounded on this success story and showcased more pipeline products which could deliver further expansion in 2020 and beyond.

Led by pharmaceutical division CEO Bill Anderson, they presented highlights from the company's late and mid-stage pipeline across its key therapy areas of oncology, neuroscience, immunology and infectious diseases and ophthalmology.

The company's financials demonstrate how comfortably it defied biosimilar-induced decline: between 2018 and the same period this

year, it lost $757m in revenues to biosimilar versions of MabThera/Rituxan (rituximab) and Herceptin (trastuzumab) in Japan and Europe, but gained $2.5bn from its new products.

Anderson added that the new products also matched the older blockbusters in terms of their profit margin. "If you hear us increasingly confident that we will go through the time of biosimilar impact, this is why," he told the investor audience.

Roche will be able to cling onto US revenues from older biologics for years to come, thanks to the uptake of biosimilars in that market being likely to remain much slower than in Europe.

This will give the company time to expand the labels of its rising stars, and get more new products approved.

KEY FILINGS

Roche identified 17 of its late-stage assets as having large sales potential. These include two set for filing this year – risdiplam for spinal muscular atrophy (SMA), which will compete with Biogen Inc.'s Spinraza (nusinersen) and Novartis AG's Zolgensma (onasemnogene abeparvovec), and satralizumab, which will challenge Alexion Pharmaceuticals Inc.'s Soliris (eculizumab) in neuromyelitis optica spectrum disorder (NMOSD).

These highlight an emerging strength of the company's neuroscience portfolio, added to by HTT-ASO, potentially the first ever disease-modifying treatment for neurodegenerative Huntington's disease. Roche says the drug will be filed by 2022, or potentially earlier if regulators agree to accept early data from ongoing Phase II and Phase III trials.

Another key filing highlighted was etrolizumab in Crohn's disease and ulcerative colitis, with a Phase III trial of the new agent in a head-to-head with standard-of-care Remicade (infliximab) underway and filing expected in 2020.

Also in Roche's immunology pipeline is a new use for its underperforming lymphoma treatment Gazyva (obinutuzumab), with the company optimistic that the drug could prove a breakthrough in lupus nephritis.

While analysts rate Roche's pipeline, it is not yet clear which ones might join Ocrevus, Tecentriq and Hemlibra in the multi-billion blockbuster bracket.

SPARK HOLD-UP

Also perplexing for investors are the repeated delays to Roche's acquisition of gene therapy pioneer Spark Therapeutics Inc. It announced in February plans to acquire Spark for $4.8bn, but since then the deal has been postponed several times, with concerns from US and UK antitrust authorities about a potential monopoly in hemophilia seen as the most likely reason.

It is natural for Roche to be conservative about including Spark in its forward view of its pipeline, but many analysts were nevertheless surprised by how little the gene therapy company's potential was touched on.

At the same time, it was also noted that the company included personalized T-cells in its oncology technology platforms, something that looks to be a u-turn, after Roche "disavowed" cell therapy, in the words of Citi analyst Andrew Baum.

The company's oncology strategy is likely to evolve further as its longstanding chief medical officer and head of global product development, Sandra Horning, steps down from the post by December this year. Her successor will be Levi Garraway, who is joining from his role as SVP of oncology R&D at Eli Lilly & Co., and will find Horning a hard act to follow. *(Also see "Roche's New Chief Medical Officer Levi Garraway Brings Deep Cancer Genomics Expertise" - Scrip, 19 Aug, 2019.)*

As well as laying out the potential of its pipeline, Anderson also restated Roche's commitment to adapting its commercial strategy to a changing pricing and reimbursement model, and embracing the digital revolution to transform processes across the business.

All the same, he was also happy to rein in expectations when necessary – such as when one investor characterized Tecentriq as a relative disappointment in immunotherapy compared with the runaway market leader, Merck's Keytruda (pembrolizumab).

"Oh, why wasn't Tecentriq first? I don't know. Your favorite team, do they win all their games? No? I think that's the answer. We strive for excellence…but we're not always going to be first in the world."

Published online 17 September 2019

Purdue's Opioid Rescue Drug Development To Continue Under A New Company

JESSICA MERRILL jessica.merrill@informa.com

Purdue Pharma LP's effort to develop an opioid overdose reversal drug – and theoretically make more money off the opioid crisis – didn't sit well with the American public, even though the company vowed it would not profit from the sale of the medicines.

Now, in the company's bankruptcy filing on 16 September, Purdue is proposing to continue the development of nalmefene hydrochloride and other products under a new company that would ultimately provide millions of doses at no or low cost.

"This proposal – which the debtors hope and believe can be life-saving – is unprecedented in scope and nature, and can be consummated only in connection with a resolution of the litigation," the bankruptcy filing says.

Purdue, which made billions selling the opioid OxyContin (oxycodone), is now developing drugs that reverse opioid overdoses and treat opioid addiction. The company has insisted the initiative is part of its commitment to helping fight the public health crisis, although the drug development has gotten some negative publicity in the general press.

The company initiated a Phase I trial, NAL 1002, testing nalmefene HCI injection in July, after the product was granted fast track designation by the US Food and Drug Administration for the emergency treatment of known or suspected opioid overdose. Initial data from the study in healthy adults is expected in the third quarter.

The company has sought to develop the drug as a generic product in vial and pre-filled syringe formats for administration by health care providers, and as an autoinjector that could be administered by family members and friends through the 505(b)(2) pathway for drugs that reference existing products.

Nalmefene HCI is an opioid antagonist like Adapt Pharma Ltd.'s Narcan (naloxone) that can restore respiration to a person who has stopped breathing as a result of overdosing, but nalmefene has a longer duration of action. Purdue says it could have the potential to reverse overdoses from synthetic opioids such as fentanyl and its analogues, which are the principal driver of opioid overdose deaths and for which existing reversal medications may not be sufficiently potent or long lasting. Multiple doses of naloxone can be required to rescue a patient, according to Purdue.

The FDA approved the first generic version of naloxone nasal spray from Teva Pharmaceutical Industries Ltd. in April, a product that can be used by people without medical training. *(Also see "Keeping Track: Approval Of First Intranasal Naloxone Copycat Highlights Otherwise Generic Week" - Pink Sheet, 19 Apr, 2019.)* Purdue outlined the strategy to continue the development of nalmefene in its bankruptcy filing, which is part of an opioid liability settlement agreement the company hopes will settle more than 2,000 outstanding lawsuits. *(Also see "Will Purdue Bankruptcy Filing Resolve 'Unrelenting Chaos' Of Opioid Litigation?" - Scrip, 16 Sep, 2019.)*

"Purdue has been advocating for a settlement that would ensure that the development of this rescue medication is completed and that the settlement is structured so that millions of doses can be distributed at no or low cost to communities across America," according to the filing.

The reality of the fallout from the public health crisis on the drug industry is beginning to take shape, with Purdue being the second drug maker to recently file for bankruptcy over opioid liability after Insys Therapeutics Inc.. *(Also see "Purdue Pharma: From Blockbuster Success To Bankrupt Villain " - Scrip, 16 Sep, 2019.)*

The new company Purdue proposes would also continue to support the development of an over-the-counter nasal naloxone product. Despite the availability of Narcan, access remains limited because of the cost to first responders and the requirement for a prescription. Purdue is working with an independent pharmaceutical company called Harm Reduction Therapeutics, to develop a low cost OTC naloxone nasal spray. HRT is seeking nonprofit status. Purdue has paid and will continue paying HRT's development costs.

Purdue is also seeking FDA approval for a generic version of Suboxone (buprenorphine/naloxone), another addiction therapy, that it would distribute at low or no cost.

Published online 17 September 2019

Cynata In Potential Japan Double As Fujifilm Acquires Lead Asset

IAN HAYDOCK ian.haydock@informa.com

In line with its strategy to build out a presence in cell and regenerative therapies, the major diversified Japanese group Fujifilm Corp. has obtained exclusive worldwide rights to develop, manufacture and commercialize Cynata Therapeutics' lead pipeline asset, CYP-001, for graft-versus-host disease (GvHD).

The agreement looks unlikely to derail a possible broader acquisition of Cynata as a company by another Japanese firm, Sumitomo Dainippon Pharma Co. Ltd. (SDP), given that the option arrangement was already openly known. Discussions on this potential agreement remain ongoing, and Dainippon made no new statement following the confirmed Fujifilm deal.

This is worth $3m upfront to ASX-listed Cynata, which specializes in cell therapeutics and was formed in 2011. Its proprietary stem cell technology platform Cymerus uses allogeneic induced pluripotent stem cells (iPSCs) taken from one banked blood donation from one adult donor to enable the derivation and economical commercial manufacture of an unlimited number of consistent mesenchymal stem cells (MSCs) for therapeutic use.

Cymerus has also shown preclinical promise across a broad range of other potential indications including asthma, diabetic wounds, heart attack and cytokine release syndrome related to CAR-T therapy.

The new CYP-001 agreement, which represents the exercise of the license option - for which the deadline had been extended to 19 September - will provide valuable additional non-dilutive funding to Cynata as it looks to progress its pipe-

line. The venture had a cash balance of around AUD7m ($4.8m) at the end of June.

The Melbourne-based firm is also planning to start Phase II trials with similar cell therapeutics in other indications, including with CYP-002 this year in critical limb ischemia and a 448-patient trial in osteoarthritis with CYP-004. The latter program would be one of the largest ever clinical trials with an MSC therapy.

CLINICAL PROMISE

GvHD is a complication that occurs after bone marrow transplants for diseases including leukemia, and the inflammatory response is ordinarily treated with steroids and immunosuppressants. However, approximately half of the patients fail to respond to such treatment.

A completed Phase I trial in steroid-resistant patients earlier this year met all clinical endpoints and showed positive safety and efficacy outcomes. The study showed a 93% overall response rate by day 100, with 14 of the 15 patients showing an improvement of at least one grade versus baseline in symptoms such as skin eczema and digestive disorders.

The study, at sites in the UK and Australia, was the first time that iPSC-derived MSCs had been explored in a clinical trial by a corporate sponsor; Fujifilm said it had decided to exercise the CYP-001 license in large part based on the positive results.

The Japanese company is now aiming to launch a Phase II trial for prevention and treatment of GvHD in Japan before the end of 2020, and will bear all costs of any further product development activities in relation to GvHD, along with responsibility for regulatory submissions and commercialization.

FINANCIAL ASPECTS

As part of the agreed deal, Cynata may receive additional future product development and commercial milestone payments of up to $43m, the first of which would be $2m on completion of the first Phase II trial in the US, UK or Japan.

Subsequent milestones include completion of Phase III trials ($3m), submission of applications for regulatory approvals ($12m), acceptance of geographic marketing authorizations and first sales ($16m) and extending the indication ($10m).

In addition, Cynata will receive a 10% royalty on all future product sales if the licensed product is successfully commercialized in any country in which any licensed patents are granted or pending. Having sub-licensed certain patent rights licensed-in from the Wisconsin Alumni Research Foundation (WARF) in respect of the Cymerus technology to Fujifilm, Cynata will be required to make a one-off cash payment to WARF of $10,000.

Cynata is also required to pay WARF a mid-single digit percentage royalty on Fujifilm product sales and 30% of other amounts received from Fujifilm, including in respect of milestone payments. Fujifilm and Cynata will enter into a separate agreement for the supply of product by Cynata for certain future development activities at cost plus a "moderate double-digit" manufacturing margin. The source iPSCs will be supplied by the US Fujifilm subsidiary Fujifilm Cellular Dynamics Inc.

To facilitate Cynata's ongoing partnering efforts, certain amendments have been made to the license agreement between Cynata and WARF, particularly in relation to sub-licenses under the WARF patents and extending certain interim development milestones, while not changing the current milestone for obtaining approval from the US FDA (or other equivalent foreign agency) in 2026.

INVESTMENT, STRATEGIC INTEREST

Fujifilm already had a financial stake in Cynata through a minority investment made in January 2017 as part of the option deal for rights to CYP-001.

More broadly, the major Japanese group has a strategic interest in cell and regenerative therapies as it diversifies away from its traditional businesses and towards the life sciences sector, where it sees good growth in demand for products, equipment and services.

The Healthcare & Material Solutions part of its business now accounts for the largest share of group sales (around 43%), and it also has a conventional drugs business in the form of subsidiary Fujifilm Toyama Chemical Co. Ltd., acquired in 2008 and with R&D interests in anti-infectives and Alzheimer's disease.

Other group companies already involved in the cell therapy field include Japan Tissue Engineering, Fujifilm Wako Pure Chemical Corporation and Fujifilm Irvine Scientific, and Fujifilm also has interests in diagnostics and imaging.

The company said it continues to advance its internal pipeline of cell therapies using products derived in particular from iPSCs, focusing on diseases with high unmet needs such as age-related macular degeneration, retinal pigment degeneration, Parkinson's disease and heart disease.

"iPSCs have the potential to offer a more flexible approach and address the issues of limited availability and inconsistent quality associated with other source materials," it noted.

POSSIBLE DAINIPPON ACQUISITION ON TRACK

In July, Cynata confirmed that it "has received an indicative, non-binding and conditional proposal" from SDP regarding a potential acquisition of all outstanding shares in Cynata (around 101.89 million) at a price of AUD2.00 ($1.41) each in cash.

Rumors around a possible acquisition have pushed up Cynata shares by 48% since the start of July, and SDP is understood to be the sole bidder.

Any possible deal would further bolster the Japanese firm's strategic interest in cell and regenerative therapies, where it is already developing an allogeneic iPSC-derived dopamine neural progenitor therapy in Japan for Parkinson's disease (Phase I/II), along with an iPSC-derived retinal pigment epithelium therapy for age-related macular degeneration (pre-Phase I).

The first commercial contributions from the push in these areas are not expected by the company until the 2023-37 period, however.

Amid the looming loss of exclusivity for its global blockbuster, the atypical antipsychotic Latuda (lurasidone), SDP is also planning to sign a definitive agreement next month for the acquisition for $3bn of Roivant Sciences Inc.'s stakes in up to 11 "vant" companies (see side box).

This would bring several late-stage candidates in female health and urology, but these drugs and areas are distinct from cell/regenerative therapy, meaning the pursuit of Cynata looks unlikely to be affected.

Published online 18 September 2019

AZ, Novartis, Roche Take Part In UK's Big Data Push

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

Seven new data hubs are to be rolled out across the UK to speed up research for new medicines and improve care for patients, with input from big pharma and tech companies.

The hubs, which will be launched on 1 October, will use the latest advances in technology to connect and analyze health data from across the National Health Service (NHS). The UK's health service holds rich data sets, but these frequently remain siloed within individual trusts and institutions and are difficult to access rapidly.

The initiative is part of a wider push to open up NHS data and research capabilities to greater collaboration with industry, seen as vital for the UK's life science sector in a post-Brexit environment.

Many of the hubs will combine genetic data with patient records and other data sources, or use AI to help diagnose conditions faster and analyze research data faster.

FOUR DISEASE AREAS

Led by the government-funded Health Data Research UK, the hubs are focused on a number of specific areas, with four dedicated to disease areas – cancer, inflammatory bowel disease (IBD), respiratory and eye health – and three more focusing on acute care, accelerating clinical trials and real world data (RWD) use. *(Also see "RWD Key To Scottish Orkambi Deal" - Pink Sheet, 12 Sep, 2019.)*

What all the hubs have in common is the aim of making NHS data more easily accessible and user-friendly for academic and commercial researchers, while also maintaining strict controls around data privacy and consent.

Andrew Morris, a doctor with a special interest in diabetes and Director of Health Data Research UK, said:

"The UK is home to some of the world's leading researchers and innovators who have historically struggled to access large scale data about people's health. Creating these hubs and the wider secure infrastructure will, for the first time, give researchers the opportunity to use data at scale to research the genetic, lifestyle and social factors behind many familiar common diseases and identify revealing data trends which may help with finding cures or treatments."

The hub focused on real world data is Discover-NOW and brings together many leading research hospitals such as London's Imperial College hospital and the Royal Marsden, along with tech companies such as Google and Medopad, and pharma companies including AstraZeneca PLC, Novartis AG, Janssen, Roche and The Medicines Co.

Richard Erwin, general manager, Roche Products Limited is taking part in the INSIGHT collaboration, focused on eye health.

"Roche is delighted to be a key part of the multi-party collaboration, establishing the first-of-its-kind holistic data-record in eye disease and oculomics, to help drive the future of eye health."

Erwin said the INSIGHT project's goals were fully aligned with the company's own personalised healthcare mission, to bring together cutting edge science with meaningful data at scale and analytics to provide patients with personalised treatment.

"As the premier health data research hub for eye health, INSIGHT is a great example of the UK being one of the best places in the world to invest in global life sciences."

Adam Higgins, Industry Partner, Discover-NOW (the hub focused on real world data) from AstraZeneca said: "We are working with some of the best medical minds in the business, some of the best technology minds in the business, and as a collective group of people we can understand how to better understand how to manage and support patients with long term conditions."

Novartis is a partner in two of the collaborations, BREATHE - the respiratory hub and Discover NOW. "By improving the way we use healthcare data in the NHS we can speed up clinical decision making, identify and address healthcare problems proactively and ultimately provide better care to patients," said Mark Toms, medical director and chief scientific officer, Novartis UK.

"At the same time, the health data research hubs will enable researchers to better understand health and disease and to research new life saving or life changing treatments," added Toms.

Another hub is DATA-CAN, focusing on research data in cancer, and aims to transform how data from oncology clinical trials are used across the UK.

One of the key commercial partners in the venture is clinical research services giant IQVIA, which is bringing its Oncology Data Network (ODN) platform to the collaboration. This is a multi-country European network which aims to reveal how cancer treatments are being used in near real time.

Tim Sheppard, IQVIA's SVP and General Manager, Northern Europe said:

"Access to data is absolutely key to attracting research and development from industry. I think the UK is in a race with other countries to develop its capabilities in this field."

He said that 80% of all clinical trials are delayed, and that the new initiative would help address some of the major problems behind these hold-ups. These include identifying and recruiting patients, and informing the design of protocols to maximize their chances of success.

"This is a really admirable program, and given the amount of energy and collaboration put into it, I think it will be successful," Sheppard concluded.

As with many NHS research initiatives, participation in the hubs is not mandatory, which means it will take a number of years for the collaborations to gain momentum.

Details about what outputs to expect from the collaboration are yet to emerge before the hubs are launched in October. However the DATA-CAN project has set itself a target of contributing to saving the lives of 30,000 cancer patients a year, through improved access to treatment and early diagnosis.

Published online 19 September 2019

Scrip Awards
Informa Pharma Intelligence

Book a Table

The 15th Annual Scrip Awards

4 December 2019 | London Hilton on Park Lane, London

www.scripawards.com

General Enquiries:
Lisa Anderberg | Tel: +44 (0) 20 7551 9560 | Email: lisa.anderberg@informa.com

Sponsorship and Table Booking Enquiries:
Christopher Keeling | Tel: +44 (0) 20 3377 3183 | Email: christopher.keeling@informa.com

Sanofi To Co-Develop Digital Therapeutic For MS Patients

JOHN DAVIS john.davis@informa.com

Sanofi has signed an agreement with New York-based Happify Health to develop a health regulator-approved digital therapeutic aimed at improving the mental health of patients with multiple sclerosis, who often exhibit symptoms of anxiety and depression.

Sanofi already has experience in the MS field through its two marketed MS therapies, Aubagio (teriflunomide) and Lemtrada (alemtuzumab), and in February appointed its chief medical officer, Ameet Nathwani, to the additional position of chief digital officer.

But perhaps more importantly, Sanofi's new CEO, Paul Hudson, has been tasked with improving the company's digital capabilities, which already include a broad partnership with Google.

Happify Health offers web and app platforms for the general public which use game-based approaches to reduce symptoms of stress, anxiety and depression, and says it has been "preparing for our entry into prescription digital therapeutics for several years." Happify's consumer app has nearly 4 million users and the company has relationships with US health plans and multinational employers.

Sanofi already has experience in the MS field through its marketed therapies, Aubagio and Lemtrada.

Sanofi says it will work with Happify Health to develop a version of that company's digital platform aimed specifically at MS patients, which will be submitted to the US FDA for clearance as a medical device.

Thought appears to have been given to development outside the US, as the agreement between the two companies is billed as global; they say the collaboration is the beginning of a long-term effort to use technology to improve outcomes in a cost-effective, accessible and patient-engaging way.

Happify Health says it uses scientific research from positive psychology, cognitive behavioral therapy (CBT) and mindfulness, and combines it with leading-edge technology, to impact everyday lives.

In a scientific study comparing the use of Happify's digital platform with what was deemed to be the usual process followed by a web user (a psycho-educational approach providing content and information without gaming-related activities), Happify's technology was associated with a greater reduction in anxiety and depression symptoms than was seen in the control arm. More than 40% of subjects were still active on the platform after 12 months, the companies say.

Sanofi is not alone in pursuing digital therapeutics, with Japan's Shionogi & Co. Ltd. being one of the latest pharmaceutical companies to express an interest.

Published online 19 September 2019

Bayer Aims To Take AI-Driven One Drop Beyond Diabetes

STEN STOVALL sten.stovall@informa.com

Germany's Bayer AG has entered into a collaboration and licensing agreement to leverage Informed Data Systems' One Drop integrated digital platform – currently used in treating diabetes – to advance the German conglomerate's bio-digital therapeutic efforts in cancer, cardiovascular disease, and women's health.

Through the licensing agreement, announced 17 September, Bayer will use One Drop's data science and predictive capabilities, and harness its mobile capabilities. "As part of our strategy to shape the future of healthcare and build new businesses in digital health, we are investing in integrated digital solutions to improve health outcomes through data driven solutions," Stefan Oelrich, Bayer's head of pharmaceuticals, said.

As part of Bayer's commitment to the AI collaboration, it has invested $20m in a Series B financing in One Drop and signed a licensing agreement worth $10m for further developing and commercializing the artificial intelligence specialist's technology platform. The Series B, led by Bayer, raised a total of $40m.

Bayer to develop One Drop's AI platform for multiple diseases

Informed Data Systems' CEO Jeff Dachis said that "as a new investor and commercial partner, Bayer is validating One Drop's superior user experience, modular and extensible product offering, and ability to bring affordable, accessible healthcare to millions of people worldwide."

One Drop describes itself as one of the fastest growing diabetes management solutions globally, with nearly 1.5 million people in 195 countries estimated to be using its technology. The One Drop app supports HealthKit, CareKit, Health Records and Siri Shortcuts on iPhone, supports Google Fit on Android, and integrates directly with Fitbit and Dexcom on both iPhone and Android devices.

The ability of One Drop's integrated platform to offer an easy and effective way for people to track and manage a variety of health conditions clearly impressed Bayer on its potential for use in therapeutic discovery and innovation.

"This collaboration allows us to obtain access to a world leading self-care platform for disease management beyond the boundaries of medicines with strong artificial intelligence-driven capabilities that could lead to better healthcare outcomes for people with chronic conditions," said Oelrich, who will join One Drop's board.

The parties said their collaboration is a sign of today's times."With demographic shifts causing an increase in chronic diseases and multiple conditions, and with public health systems already facing cost pressures, data-driven, digital technology is transforming how patients access quality healthcare more effectively and at a lower cost," Dachis claimed.

"We are looking forward to partnering with Bayer to help patients worldwide manage conditions like cancer and heart disease." *Published online 18 Sept 2019*

Novo Anticipates Q4 Soft Launch For Closely Watched Oral GLP-1 Agent Rybelsus In The US

MANDY JACKSON mandy.jackson@informausa.com

Fourteen years after the first approval of an injectable glucagon-like peptide-1 (GLP-1) agonist for the treatment of type 2 diabetes, Novo Nordisk AS won US Food and Drug Administration for the first oral GLP-1 agent – Rybelsus (semaglutide) – on 20 September.

Novo Nordisk US chief medical officer Todd Hobbs told *Scrip* in an interview that the company anticipates a soft initial launch in the fourth quarter of this year while sales teams are trained to market Rybelsus according to its label, as manufacturing is ramped up to meet commercial demand and while reimbursement negotiations with US payers to secure patient access continue. The company believes that more diabetes patients will be offered treatment with a GLP-1 agent now that physicians, particularly primary care doctors, have an oral drug to prescribe.

The US FDA approved Rybelsus 7mg and 14mg tablets as a once-daily therapy in combination with diet and exercise to reduce blood glucose in adults with type 2 diabetes, based on results from the PIONEER clinical trial program, which enrolled 9,543 patients in 10 studies and included head-to-head trials against Merck & Co. Inc.'s oral dipeptidyl peptidase-4 (DPP-4) inhibitor Januvia (sitagliptin), Eli Lilly & Co./Boehringer Ingelheim International GmbH's oral sodium-glucose co-transporter 2 (SGLT2) inhibitor Jardiance (empagliflozin) and Novo's once-daily injectable GLP-1 agent Victoza (liraglutide).

MAKING THE GLP-1 CLASS MORE ACCESSIBLE

The first GLP-1 agonist – AstraZeneca PLC's Byetta (exenatide), originally developed by Amylin Pharmaceuticals Inc. – was approved in the US in 2005 and Victoza has been on the market since 2010. However, Hobbs noted that while GLP-1 drugs have been able to safely lower blood glucose and reduce weight in diabetes patients – and have shown a reduction in cardiovascular risk – uptake has been limited by the fact that they are injectable therapies, despite inclusion in treatment guidelines from the American Diabetes Association (ADA) and other medical groups.

"In particular, if you look at the most recent treatment guidelines from ADA – and even at the [European Society of Cardiology (ESC)] meeting recently – and all of the cardiovascular associations, they basically favor SGLT2 inhibitors and GLP-1 agonists early and even right with metformin or first-line after metformin," Hobbs said. "That's where we really think that oral semaglutide is going to be able to move the use of GLP-1 earlier up into that area of the diabetes treatment cascade."

Data from the Phase III PIONEER 6 trial presented at the ADA meeting in June showed a 21% reduction in major adverse cardiovascular events (MACE) with Rybelsus, although the result versus placebo was not statistically significant. Nevertheless, the study showed that the oral drug appears to be safe for diabetes patients at high risk of cardiovascular events.

Novo Nordisk is running a larger cardiovascular outcomes trial for Rybelsus, but it already has filed supplemental applications with the US FDA seeking label claims that semaglutide and the company's once-weekly injectable GLP-1 agonist Ozempic (semaglutide) – first approved in December 2017 – reduce the risk of MACE. Decisions on those applications are expected in the first quarter of 2020.

Hobbs noted that an FDA-approved label claim regarding MACE reduction would make doctors more comfortable prescribing Rybelsus, help payers give the product more favorable placement on their formularies, and boost the drug's status in treatment guidelines.

"The data has been published and ADA and other guidelines have looked upon semaglutide favorably, but we clearly think it's important to have it in the label and get the FDA's blessing on the data and the benefit," he said. "We are also conducting several outcomes studies, one of which is a cardiovascular outcomes trial with oral semaglutide, so if for some reason we don't get the indication with this application, we're going

TURN TO PAGE 14

DENMARK'S LIFE SCIENCES INDUSTRY

Focused On Continued Growth

Denmark's life sciences industry plays a key and growing role in the Danish economy, generating just over 17% of total exports in 2018, or DKK115bn, up from DKK107bn in 2016 and DKK54bn in 2008.

Conversion rate: $1 = 6.80 DKK

The Danish life science industry's ambition, actively supported by the Danish government, is now to double that export contribution by 2025.

To make that happen, Denmark's government in the spring of 2018 devised and passed through parliament a so-called Growth Plan for Life Science, comprising 36 policy initiatives.

The policy aim is to strengthen future R&D standards and opportunities in the country by increasing the availability of strategic research funds for life science.

Denmark's three largest pharma companies by net sales in 2018:

Novo Nordisk / DKK111.8bn
Lundbeck / DKK18.1bn
Leo Pharma / DKK10.4bn

Conversion rate: $1 = 6.80 DKK

Steps taken include an increase in companies' tax deductions for research and development expenses, up from 100% to 110%.

The growth plan also saw establishment of Trial Nation, a public-private partnership between the life sciences sector and all Danish hospitals, with the purpose of increasing research and clinical trials in Denmark. It reflects the interest of public healthcare authorities in stimulating stronger research in Denmark and supporting shorter time to market for new pharmaceuticals and medical technology.

Another initiative is the increased focus on high quality approval processes for new pharmaceuticals at the Danish Medicines Agency (DKMA).

Over the next few years, the DKMA will further increase its staff with more scientific advisors, especially within the field of data analytics, and strengthen international cooperation even further.

The DKMA's initiatives will mean faster introduction of new products for the industry, due to the possibility of early submission with Real World Data in a high-quality approval and services process, which is well connected to medical agencies in other countries.

Companies have also been exempted from paying state fees previously incurred when conducting Phase I trials in Denmark.

Denmark

- Is the most digitalized country in the EU
- Has electronic healthcare data going back more than 40 years
- Boasts a high level of trust among Danish citizens in the public authorities, helping to make Denmark the no. 1 country in Europe for clinical trials, as measured by trials conducted per capita.
- Denmark's social security number system, a unique patient identifier called CPR, makes it possible to combine specific patient data for research with data from a vast database of 5.8 million Danes.

Sources: Danish Industry Ministry; Healthcare Denmark

Credit: Gayle Rembold Furbert & Jean Marie Smith | Design | Pharma Intelligence

CONTINUED FROM PAGE 11

to generate further data to explore it in greater detail in the future."

Applications seeking approval for Rybelsus to treat adults with diabetes are under review in Europe, Japan and other ex-US markets.

US LAUNCH WILL HAVE A SLOW START

Hobbs noted that there are a lot of moving pieces involved in the US launch of Rybelsus, including manufacturing adequate supplies of the product, reimbursement negotiations with payers, and training that ensures sales representatives are prepared to market the drug in line with its label and the data generated in the PIONEER studies.

Because those efforts are ongoing, he said there will be a "soft, limited launch within a month or so" and a full launch in the first quarter of 2020.

Initial supplies of Rybelsus will come from Novo's manufacturing facilities in Denmark, but the company is bringing a manufacturing site online in Clayton, NC, and it acquired a tableting and packaging facility in Durham, NC earlier this year to supply the US market.

While the company still is negotiating reimbursement from US payers, Novo already has established a savings card program for patients with commercial insurance to reduce their out-of-pocket costs for Rybelsus to as little as $10 per month.

The drug's list price will be revealed within the next few business days, but Hobbs said it will be competitive with other GLP-1 agonists.

Novo's first- and second-generation GLP-1 drugs Victoza and Ozempic garnered a 53% share of new GLP-1 agent prescriptions in the US as of the second quarter of this year. Ozempic's sales exceeded analyst expectations at $349m in the second quarter – a needed boost as the company experienced a decline in sales for its blockbuster Victoza, which will face generic competitors in 2023.

"We continue to believe the company faces a fine balancing act in pricing [Rybelsus] to enable broad access, whilst minimizing market disruption and impact on its existing highly profitable injectable franchise," Deutsche Bank analyst Richard Parkes said in a 20 September note.

> "It makes most sense to us to price Rybelsus close to injectable GLP-1s and gradually increase rebating to expand market access." – Richard Parkes

"It makes most sense to us to price Rybelsus close to injectable GLP-1s and gradually increase rebating to expand market access," Parkes added. "However, it remains possible that payers will be reluctant to provide broad access to an oral drug without meaningful rebates versus injectable drugs that naturally address a more limited patient population due to patient reluctance to initiate injectables."

The Deutsche Bank analysis viewed other investment banks' Rybelsus sales projections as close to best-case scenarios. Indeed, Jefferies analyst Peter Welford acknowledged in a 20 September note that its peak sales estimate of $7.2bn is above consensus forecasts.

Welford said he anticipates a Rybelsus list price closer to injectable GLP-1 agents with a pre-rebate cost of more than $700 per month versus pricing of about $770 for Ozempic and $920 for Victoza.

DOSING REQUIREMENTS ALSO A CHALLENGE

In addition to pricing, Rybelsus uptake also could be challenged by strict requirements for when and how patients take the drug – with no more than 4oz of water at least 30 minutes before eating or drinking anything or taking another oral medication.

Hobbs said he was worried about that issue when Novo first kicked off clinical trials for Rybelsus, but noted that the pill's efficacy in those studies wiped out any fears he had that patients wouldn't be able to take Rybelsus as directed and therefore wouldn't benefit from treatment. In fact, in pricing and reimbursement negotiations, payers have responded to the potential for improved adherence to GLP-1 therapy with an oral drug.

Jefferies analyst Welford also noted that prescribers are interested in an oral option as evidenced by standing room-only attendance at Rybelsus data presentations during the recent European Association for the Study of Diabetes (EASD) meeting in Barcelona.

"The symposium panel and presenters mused whether oral semaglutide could increase acceptance of GLP-1s amongst physicians and patients, and change GLP-1 prescribing habits, particularly amongst primary care physicians, and potentially also make GLP-1 use more frequent and bringing it earlier in the treatment paradigm," Welford wrote.

However, the Rybelsus label has a boxed warning about a potentially increased risk of thyroid C-cell tumors and it notes that the drug is not recommended as a first-line treatment for type 2 diabetes.

Rybelsus should not be prescribed to patients who previously have had medullary thyroid carcinoma (MTC) or have a family history of MTC. It also shouldn't be prescribed to patients who have ever been diagnosed with multiple endocrine neoplasia syndrome type 2 (MEN 2). Other safety warnings include pancreatitis, diabetic retinopathy, hypoglycemia, acute kidney injury and hypersensitivity reactions.

The most common side effects in clinical trials were nausea, diarrhea, vomiting, decreased appetite, indigestion and constipation.

Published online 22 September 2019

Rybelsus, Other Treatment Improvements For Chronic Disease Have OptumRx's Attention: **https://bit.ly/2mdp776**

Emmaus Fumes After EMA Rejects Sickle Cell Drug Again

KEVIN GROGAN kevin.grogan@informa.com

Emmaus Life Sciences Inc. has ripped up its European filing of Xyndari, which is approved in the US, after the continent's regulators once again recommended against approving the sickle cell drug.

Rip it up and start again: Emmaus looks at new option to get Xyndari approved

The US firm, which was delisted from the NASDAQ last week, has announced the withdrawal of its marketing authorization application to the European Medicines Agency for Xyndari, a prescription grade version of the amino acid supplement L-glutamine, for the treatment of sickle cell disease. The file has been pulled after it became clear that the EMA's drug evaluation committee, the CHMP, was sticking to its initial opinion that the submission did not demonstrate that Xyndari was effective at reducing the number of sickle cell disease crises or hospital visits.

In May, the CHMP issued a negative opinion on Xyndari, stating concerns about Emmaus's main study involving 230 patients with the inherited blood disorder. It said that "a large number of patients, more who were taking Xyndari than taking placebo, dropped out of the study before it was finished, and information on how the medicine worked for those patients was not available. The CHMP considered that the way data from these patients were dealt with was not appropriate."

The committee was also not convinced about a supportive study, noting that in the latter, more of the patients taking Xyndari had received a sickle cell medicine - hydroxyurea - than patients taking placebo. "This could have influenced the results," the CHMP claimed.

Being knocked back again on the drug, which was approved in the US for sickle cell in 2017 on the same data set, has proved too much for Emmaus. CEO Yutaka Niihara said, "Because we have demonstrated the efficacy of Xyndari, as supported by the data from the trials conducted, we are disappointed in the CHMP's position."

In a direct challenge to the EMA, he went on to say that "we are seriously considering a decentralized approval procedure on a country by country basis." This would involve Emmaus asking a European Union country to act as a reference member state (RMS) to do an initial evaluation of Xyndari and issue a draft report.

Other EU member states would then either agree with the RMS's review or ask further questions. If all the issues were resolved, each member state could then issue a marketing license for the product.

Niihara went on to say that Emmaus "will continue to endeavor to broaden our global patient base, while identifying new clinical uses for L-glutamine, obtaining additional patents and distribution partners, and through ongoing community and physician outreach." Outside the US, Xyndari is supplied through early access programs based on named-patient use in a number of EU member states, Turkey, and countries in the Middle East and South America.

Emmaus, which completed a reverse merger with MYnd Analytics in July, had sales for the first six months of 2019 of $11.2m, up from $3.4m for the same period last year. The firm said the rise was driven by "the continuing roll-out and market acceptance of Endari; it is also conducting studies looking at the potential of the drug as a new treatment option for patients with the digestive condition diverticulosis and type 2 diabetes.

The first new sickle cell drug to launch in the US in nearly 20 years, Endari has got off to a slow start. However, in a recent interview with *Scrip*, Niihara said the company is making substantial progress on the drug's commercialization. "Physicians, providers and patients are very happy with Endari. "We hear stories like, 'Now I can go to school, now I can stay at work, I don't have to go to the hospital anymore.'"

Nevertheless, competition is on the way. Global Blood Therapeutics Inc.'s new drug application for voxelotor was recently accepted by the US Food and Drug Administration with a priority review and a target action date of 26 February. Novartis AG filed its monoclonal antibody crizanlizumab in the US and the EU in July for the prevention of vaso-occlusive crisis in sickle cell patients.

These are tricky times for Emmaus. Its shares sank over 38% to close at $2.77 on 10 September after a NASDAQ hearings panel declined to reverse a decision taken in July to delist the stock. The panel found that the company was not compliant with its listing rules, including a $5m minimum stockholders' equity requirement.

Emmaus cited a letter from the panel as saying that it "recognized that the company is doing important work and expressed its hope that Emmaus securities may again trade on NASDAQ."

Published online 20 September 2019

US FDA AdComm Win For Aimmune's Palforzia Bodes Well For DBV's Peanut Allergy Patch

SUE SUTTER sue.sutter@informa.com

A US Food and Drug Administration panel's positive review of Aimmune Therapeutics Inc.'s peanut allergy oral immunotherapy Palforzia would seem to bode well for DBV Technologies SA's epicutaneous immunotherapy Viaskin Peanut, assuming the latter's resubmitted application is up to snuff on manufacturing and the firm is prepared with a Risk Evaluation and Mitigation Strategy.

Although some analysts see the DBV patch product as having a more attractive safety profile than Aimmune's Palforzia, the recent advisory committee review's focus on a restrictive Risk Evaluation and Mitigation Strategy (REMS) for the oral immunotherapy may be an indication DBV should be prepared on the REMS front as well.

In the case of Palforzia, however, analysts do not expect the REMS requirements will be a rate-limiting factor to adoption in a potential $1bn market that currently lacks an approved, standardized treatment for peanut allergy.

On 13 September, the Allergenic Products Advisory Committee endorsed the efficacy and safety of Palforzia (peanut, *Arachis hypogaea*, allergen powder for oral administration) by votes of 7-2 and 8-1, respectively.

Aimmune is seeking approval to reduce the incidence and severity of allergic reactions, including anaphylaxis, after accidental exposure to peanut in patients ages 4-17 years with a confirmed diagnosis of peanut allergy.

Given the advisory committee's nod, the agency appears on track to approve Palforzia by the end of January.

That timeline will give the FDA and Aimmune four months to reach agreement on the specifics of a REMS that the agency has deemed necessary to mitigate the risk of systemic allergic reactions, including anaphylaxis.

IN PURSUIT OF A STANDARDIZED TREATMENT

Peanut allergy is the most common food allergy in the US, affecting approximately 2% of children.

The current standard of care is strict peanut avoidance and management of symptoms with antihistamines or epinephrine following accidental exposure. However, avoidance is difficult, and accidental exposures resulting in allergic reactions are common.

Although some allergists offer oral immunotherapy, these unregulated products are typically formulated in physicians' offices using commercial food product, and they vary by dosage and treatment protocol.

"We need a defined therapy so patients and physicians know what to expect in terms of outcomes and side effects" from oral immunotherapy, Aimmune consultant James Baker, director of the food allergy center at the University of Michigan, told the advisory committee.

In the pivotal Phase III PALISADE trial, Palforzia (also known as AR101) met the prespecified success criterion on the primary endpoint – the proportion of patients ages four to 17 years in the intent-to-treat population who tolerated a dose of at least 600mg of peanut protein, with no more than mild symptoms, at the double-blind, placebo-controlled food challenge at the end of the maintenance period. The treatment difference between Palforzia and placebo was 63.2%. *(Also see "Aimmune Accelerates Commercial Planning For Peanut Allergy Drug " - Scrip, 20 Feb, 2018.)*

However, in controlled trials, Palforzia was associated with a higher rate of systemic allergic reactions and rescue epinephrine use compared with placebo.

The drug is proposed to be given in three dosing phases: initial dose escalation from 0.5mg to 6mg in a single day; up-dosing every two weeks for 24 weeks; and maintenance dosing of 300mg a day. In the clinical trial, the initial dose escalation and each new step-up in dosing were administered in the clinic under observation.

In the controlled safety population, 9.4% of subjects taking Palforzia reported systemic allergic reactions during initial dose escalation and up-dosing combined, compared to 3.8% of subjects in the placebo group. During the maintenance dosing phase, 8.7% and 1.7% of Palforzia and placebo subjects, respectively, reported systemic allergic reactions.

In the controlled safety population, epinephrine use to treat systemic allergic reactions was reported by 6.1% of Palforzia recipients and 3.1% of placebo recipients during initial dose escalation and up-dosing combined. During the maintenance phase, epinephrine use to treat systemic allergic reactions was reported by 6.1% and 1.7% of Palforzia and placebo subjects, respectively.

Aimmune and its experts said some allergic reactions are expected with daily dosing of an oral immunotherapy. However, the risks of Palforzia are well characterized, and frequency of allergic reactions declined the longer that subjects were on the therapy, the company said. *(Also see "Aimmune's Peanut Allergy Immunotherapy Brings Safety Concerns To US FDA Panel" - Pink Sheet, 11 Sep, 2019.)*

VOLUNTARY VS. REQUIRED RISK MANAGEMENT MEASURES

Aimmune proposed a voluntary risk management plan that included the following:

- Initial dose escalation and the first dose of each up-dosing level be administered in a facility equipped to treat systemic allergic reactions;
- Patients have a valid prescription for injectable epinephrine prior to initiation of Palforzia;
- Drug distribution limited to specialty pharmacies; and
- Packaging designed so that patients only receive their appropriate dose.

However, the agency appears to have deemed the voluntary plan insufficient. In framing the voting question on safety, the agency said it would require a REMS with the following elements to assure safe use:

- Documentation that any patient prescribed Palforzia has a valid prescription for injectable epinephrine;
- Caregiver/patient attestation to carry injectable epinephrine while on Palforzia; and
- A requirement that initial dose escalation and the first dose of each up-dosing level be administered in a certified facility capable of treating system allergic reactions.

Some committee members did not think the agency's REMS proposal went far enough and pushed for additional measures. These included: informed consent; documentation that patients and their families understand they are to continue to avoid eating peanut-containing products; and guidance on missed doses.

Panelists also discussed the need to clearly spell out when epinephrine should be administered, as well as the recommendation that patients avoid certain activities, such as exercising or taking a hot shower, shortly after dosing to reduce the risk of experiencing an allergic reaction.

FDA officials said the REMS was still under discussion with the company. However, labeling would include a boxed warning on the risk of systemic allergic reactions as well as a patient Medication Guide.

In a statement after the meeting, Aimmune said it proposed a boxed label warning consistent with immunotherapies to treat allergic conditions.

"Patient safety has been central to us since the beginning of the Palforzia development program. We are gratified to be aligned with FDA in our focus on patient safety," Aimmune president and CEO Jayson Dallas said in the statement. "We look forward to working with the agency to finalize our proposals, which we believe will support the safe and appropriate use of Palforzia."

PANEL OUTCOME AS EXPECTED

In the analyst community there appeared to be little surprise at the outcome of the advisory committee.

In a 13 September note, Credit Suisse analyst Evan Seigerman said the REMS requirements being discussed were "reasonable."

"Panelists generally agreed that education of patients, caregivers and providers is a necessary component for approval, and discussed ways to incorporate this and other safeguards into a potential REMS strategy to minimize risk," he said.

In a 16 September note, JMP Securities analysts said they were not surprised that Aimmune and the FDA will further define the REMS plan to incorporate some of the committee's feedback on optimal conditions for use and symptoms warranting rescue epinephrine.

"AIMT has already made strides in this area with a field team in place to provide allergist support for optimal Palforzia administration, and combined with the strong motivation for a therapy in the peanut allergy community, we do not see a rigorous REMS as a major gating factor going forward," the JMP analysts said.

Rather, "the key debate now in our minds is the size of the commercial opportunity" which "could be in the $1bn range, mostly coming from the US, driven by the significant size of the food allergy market, with 6m kids affected in the US alone," the analysts said.

SEEING VIASKIN IN THE REAR VIEW MIRROR

Aimmune may have the market to itself only for a short period of time before another competitor launches.

DBV's Viaskin Peanut is an electrostatic patch containing solubilized antigen in a condensation chamber, where it can be captured by Langerhans cells in the upper epidermis. Like Palforzia, Viaskin Peanut holds both fast track and breakthrough therapy designation.

DBV submitted the biologics license application (BLA) on 6 August after withdrawing the original submission in December due to the need to provide additional information on manufacturing procedures and controls. The company told *Scrip* it expects to hear around 5 October whether the BLA is accepted for review.

The BLA seeks approval for treatment of peanut-allergic children ages four to 11 years old. However, Viaskin Peanut missed the primary endpoint in the Phase III PEPITES trial.

Although a statistically significant greater proportion of patients treated with Viaskin Peanut had an increase in the amount of peanut protein required to elicit an allergic reaction during the food challenge compared with placebo (treatment difference = 21.7%), the primary endpoint, which evaluated the 95% confidence interval in the difference in response rates between the active and placebo arms, did not reach the prespecified 15% lower bound threshold.

Yet, some analysts believe Viaskin may bring a better safety profile.

The company reported a low rate of treatment-related epinephrine use (2.9% treatment group vs. 0.8% placebo group) in PEPITES. There were 10 cases in eight Viaskin Peanut patients (3.4%) of possibly or probably treatment-related anaphylaxis.

When asked whether it submitted a REMS with its BLA, the company said it was not able to discuss the contents of its application.

In a 15 September note, Morgan Stanley analysts saw three key positives from the Palforzia advisory committee for Viaskin Peanut's prospects.

"We think there was a clear consensus that peanut allergy presents a true unmet need that providers & patients would like to address with a safe & effective therapy," analysts Vikram Purohit and Matthew Harrison said.

"We found that the panel maintained an intense focus on safety, an area in which Viaskin Peanut has been differentiated," the analysts said. In addition, approval of Palforzia "would help define a regulatory pathway for future peanut allergy treatments including Viaskin Peanut."

While the panel was overall a positive for DBV, the agency's decision to accept or reject the Viaskin Peanut resubmission remains a key overhang, the Morgan Stanley analysts said.

In a 13 September note, SVB Leerink analysts said the panel's acceptance of the Palforzia pivotal trial's use of an oral food challenge endpoint bodes well for DBT because this was the primary efficacy endpoint in the PEPITES trial.

"Given the robust efficacy data of Palforzia, however, the read through to DBVT is somewhat less clear as Viaskin Peanut ... did not meet the pre-specified criterion for a positive trial result," the analysts said.

Nevertheless, given that DBV's epicutaneous immunotherapy leverages a different modality with a potentially better safety profile and added convenience, "we remain optimistic that with the resubmitted BLA, panelists and regulators will be receptive to Viaskin Peanut."

Published online 18 September 2019

Breakthrough Designation Confirms Gazyva Promise In Lupus Nephritis

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

The potential for Roche's Gazyva (obinutuzumab) to become the first ever approved treatment for lupus nephritis has received a boost with a breakthrough therapy designation from the US Food and Drug Administration.

The company confirmed the designation on 18 September, indicating the FDA's support based on compelling data from Roche's Phase II NOBILITY trial, unveiled in June. The breakthrough designation is good news for Roche, which has been trying to develop a treatment for lupus nephritis for over a decade – and encouraging for people with the condition, for whom there is currently no approved treatment.

It's also promising for Gazyva revenues, which has been slow to build market share as a successor to Roche's blockbuster MabThera/Rituxan (rituximab) in chronic lymphocytic leukemia (CLL) and follicular lymphoma (FL).

Lupus nephritis is a severe and potentially life-threatening manifestation of systemic lupus erythematosus (SLE), the broader condition which many companies have also tried and failed to treat with new products.

An inflammation of the kidneys, proliferative lupus nephritis carries with it a high risk of end-stage renal disease and death.

The condition overwhelmingly impacts women, particularly young non-white women: African-American, Hispanic, Native American and Asian-American women are two to three times more likely than Caucasian women to get lupus.

Consequently, Roche aimed to recruit as many of these patients to its NOBILITY study as possible, with around half of those on the Phase II trial from these

Roche has been trying to develop a treatment for lupus nephritis for over a decade.

ethnic backgrounds. The NOBILITY study met its primary endpoint, showing Gazyva, in combination with standard of care (mycophenolate mofetil or mycophenolic acid and corticosteroids), demonstrated enhanced efficacy compared to placebo plus standard of care alone in achieving complete renal response at one year.

Gazyva met key secondary endpoints showing improved overall renal responses (complete and partial renal response) and serologic markers of disease activity as compared to placebo.

The drug was among those highlighted as potential growth drivers by the company at its recent Pharma Day for investors in London. Pharma division chief Bill Anderson said the company had persisted with the drug despite complete failures of MabThera/Rituximab and Ocrevus (ocrelizumab, approved for multiple sclerosis) in the disease. While all three drugs bind to CD20 on B cells, Gazyva's mode of action differs from the other drugs, and it is able to penetrate into the renal tissue more effectively.

The condition affects about 165,000 people in the US and five biggest EU markets, representing a potential major new orphan drug market for Roche. More than 20% of patients progress to end-stage renal disease, requiring dialysis within 15 years of diagnosis, and if the drug can demonstrate this can be prevented or delayed, it will be a major step forward for treatment.

Roche plans to begin enrollment in a phase III trial in 2020, and says it is talking with regulators about how best to proceed.

In the first of half of 2019, Gazyva brought in CHF241m ($247m), up 36% on the same period last year, but still only representing 1% of the group's total revenues. However, a lupus nephritis approval could help at least double the drug's potential peak revenues.

Among the notable potential competitors for Gazyva in the space is AstraZeneca PLC's anifrolumab. A type I interferon receptor antibody, the drug recently hit its endpoint in reducing disease activity in SLE in its Phase III TULIP 2 trial.

AZ's TULIP program includes a Phase III long-term extension trial in SLE and a Phase II trial in lupus nephritis.

Specialist biopharma company Aurinia Pharmaceuticals Inc. has voclosporin, a dual action immunosuppressant drug in Phase III trials, with primary data analysis expected in Q4 2019.

Published online 19 September 2019

Novartis Says SMA Baby Death Not Due To Zolgensma

KEVIN GROGAN kevin.grogan@informa.com

Novartis AG has presented more data showing the long-term benefits of its spinal muscular atrophy treatment Zolgensma and revealed that the death of a baby in one of its trials was not caused by its one-time gene therapy.

In April, the company reported the death of a symptomatic six-month-old SMA Type 1 patient in the Phase III STR1VE-EU study, telling *Scrip* that preliminary findings indicated this occurred in the context of a severe respiratory infection followed by neurological complications. This "was deemed possibly related to treatment by the investigator," Novartis said at the time, adding that an autopsy had been performed and results were pending.

The company has now said that according to the coroner's report, the immediate cause of death was hypoxic-ischemic brain damage with respiratory tract infection as the underlying cause and these were "considered unrelated to the gene therapy by the investigator." SMA Type 1, the most severe form of the disease, was indicated as the underlying cause for the respiratory tract infection, and Novartis added that "there was no evidence of an inflammatory CNS process or a toxic or a treatment-related brain damage."

The final autopsy report did indicate that Zolgensma, the world's most expensive therapy, could have potentially contributed to the concurrent events of abnormal liver function and blood tests, as well as low blood pressure, but those were not unexpected.

The findings should ease concerns about the safety of Zolgensma at a time when Novartis finds itself under scrutiny from the US Food and Drug Administration and the country's politicians over manipulation of preclinical safety data on the gene therapy. The company was aware of the latter issue in March this year and investigated the matter internally but did not inform the FDA until June, a month after Zolgensma was approved in the US.

Despite the furore over how Novartis handled the data manipulation issue, the FDA said in August when it brought the matter to light that it believed Zolgensma was safe and should remain on the market. The company will be hoping that the positive data it presented at the European Paediatric Neurology Society (EPNS) congress in Athens on 19 September will turn the spotlight on the gene therapy for the right reasons.

Speaking to journalists ahead of the meeting in Greece, Olga Santiago, chief medical officer of Novartis's gene therapy unit AveXis, acquired last year for $8.7bn, highlighted new interim data from the SPR1NT study in children aged less than six weeks.

SPR1NT DATA

As of 30 May, of the babies who had two or three copies of the SMN2 gene (n=22) all had normal swallow function and were fed exclusively by mouth and were free of permanent ventilation. Of patients with two copies of SMN2, six (60%) were able to sit without support for at least 30 seconds at an average age of 7.6 months. Three of these patients were able to stand with assistance at an average age of 10.1 months, Santiago noted, adding that the natural history of untreated patients with SMA indicates that patients with two copies of SMN2 will never sit without assistance.

> "We are seeing further robust evidence of the potential of gene therapy to effectively halt motor neuron loss, help patients achieve motor milestones and alter the course of SMA with a one-time treatment."
> – Eugenio Mercuri

Three serious treatment-emergent adverse events were reported in three patients - croup, lethargy and hypercalcemia - but all were resolved and considered unrelated to treatment. Santiago said the data showed that "early invention before symptoms arise is critical for improved outcomes consistent with age-appropriate motor milestone gain," such as crawling, sitting and standing.

AveXis CEO Dave Lennon added that the introduction of neonatal screening in the US for SMA and other rare diseases has been an important advance for early diagnosis "and we don't have to wait for symptoms to develop." However, most countries in Europe do not offer it, Novartis noted.

STR1VE UPDATE

Santiago also updated results from the global STR1VE study in SMA Type 1 patients who are less than six months old. Eleven patients (50%) in the STR1VE-US trial and two patients (6%) in the STR1VE-EU study achieved the ability to sit without support for at least 30 seconds, an achievement babies with SMA Type 1 never reach in the natural history of the disease.

Five of the six patients in the US who reached 18 months of age (study completion) had achieved the milestone of sitting independently for 30 seconds and one of them could pull to a stand and walk with assistance.

"These updated data reinforce what we have seen in other Zolgensma studies, including survival of children with SMA type 1 who would have in the past died or required permanent ventilation before the age of two," commented Eugenio Mercuri of the Catholic University in Rome, one of the STR1VE investigators. "We are seeing further robust evidence of the potential of gene therapy to effectively halt motor neuron loss, help patients achieve motor milestones and alter the course of SMA with a one-time treatment."

Published online 20 September 2019

Ten Strategies For Success In Antibody-Drug Conjugate Development

ELEANOR MALONE eleanor.malone@informa.com

Nearly 20 years since the first antibody-drug conjugate was launched, there are still only six on the market. Recent scientific advances have improved the outlook, though, and R&D is picking up pace.

Bringing an antibody-drug conjugate (ADC – an antibody linked to a therapeutic payload) to approval offers the opportunity to participate in markets with high demand for improved treatments. The specificity of the monoclonal antibody (the targeting component of the product) helps identify patients most likely to respond, and significantly reduces off-target effects compared with conventional chemotherapy. Patients also tend to take longer to develop resistance to ADCs than to their constituent MAb, enabling them to remain on treatment for longer with better therapeutic outcomes.

It's still complex and expensive to develop ADCs, but there have been improvements in ADC platforms and linker technologies. This, together with the potential for new applications such as combination approaches with immunotherapy and chemotherapy, is fuelling pipeline expansion.

Here's a 10-point checklist to help you maximize the opportunity for success.

Antibody-Drug Conjugates Quick Facts

ADCs comprise an antibody, a linker and a payload. The antibody targets the drug to antigens on specific cells, where the linker releases the cytotoxic payload for targeted effect.

The six marketed ADCs, with dates of first approval are:

- 2000 (US): Mylotarg (Pfizer) for acute myeloid leukemia*
- 2011 (US): Adcetris (Seattle Genetics/Takeda) for Hodgkin's lymphoma, T-cell lymphoma
- 2013 (US): Kadcyla (Roche/Genentech) for HER2+ breast cancer
- 2017 (EU): Besponsa (Pfizer) for B-cell precursor acute lymphoblastic leukemia
- 2018 (US): Lumoxiti (AstraZeneca/Innate Pharma) for hairy cell leukemia
- 2019 (US): Polivy (Roche/Seattle Genetics) for diffuse large B-cell lymphoma

*Mylotarg was withdrawn in the US in 2010 because of toxicity, but re-approved in 2017 at reduced dosage.

Of just under 150 completed trials, 53% met their primary endpoint(s), 35% were of unknown or indeterminate outcome, and 12% failed.

More than 125 companies worldwide are developing antibody-drug conjugates (ADCs).
There are about 250 novel products in preclinical and clinical development.
Nearly 100 distinct targets are being evaluated.

- ~80% of ADC candidates are being assessed in solid tumor indications
- ~18% of ADC candidates are being assessed in hematological malignancies
- ~1% of ADC studies are in non-oncology indications

An increasingly common ADC development strategy is to evaluate ADC candidates in combination with other cancer treatments, including immune checkpoint inhibitors.

1. HIT THE RIGHT TARGET

The least risky approach is to go for an already validated therapeutic target, such as HER2. If you already have an approved monoclonal antibody for a therapeutic target, developing an associated ADC makes sense as a life cycle management strategy. Roche, for example, will offset declining sales of its blockbuster breast cancer MAb Herceptin (trastuzumab) – which now faces biosimilar competition – with revenues from Kadcyla (trastuzumab emtansine), which conjugates Herceptin to the chemotherapy emtansine. For others, selecting a validated target offers the opportunity to piggyback on the success of existing drugs.

2. GO FOR BROAD APPLICABILITY

Pick a high-prevalence target with broad applicability across a range of oncology – and potentially non-oncology – targets. Ideally the target antigen should be highly expressed on tumor cells and largely absent on non-tumor cells to minimize toxicity. HER2 and CD22 are good examples – but also attract more competition.

3. GO NICHE

Target a niche disease with high unmet need and the barriers to entry are much lower. It's easier to demonstrate efficacy and there's less competition, as well as a better chance of securing market access and reimbursement. AstraZeneca PLC's Lumoxiti (moxetumomab pasudotox-tdfk) is a case in point: it's the first new treatment in 20 years for relapsed/refractory hairy cell leukemia, a disease for which there are few options for relapsed patients. Nevertheless, overall sales will be limited in smaller patient populations.

4. DESIGN YOUR ADC VERY CAREFULLY

Do your research carefully when choosing the cytotoxic payload and linker. It's important to design an ADC with the right drug-to-antibody ratio (DAR): too low and it has reduced potency, too high and it may increase toxicity or impact pharmacokinetics.

5. REMEMBER YOUR BIOMARKER

Find a reliable biomarker to identify the patients most likely to benefit from the therapy, and develop a robust companion diagnostic to improve your chances of reimbursement. However, be careful: predictive biomarkers can also reduce the eligible population and hence the revenue potential.

6. MANAGE TOXICITY

ADCs are less toxic than conventional cancer chemotherapy but toxicity can still be a challenge. Watch for dose-limiting hematologic, hepatic, neurologic and ophthalmic toxicities. Because the development of resistance to ADCs takes longer than conventional MAbs, accumulated toxicity may be a greater risk and managing long-term side effects should be an important consideration.

7. STAND OUT FROM THE CROWD

Your ADC needs to be sufficiently different from existing standards of care to optimize access, uptake and pricing. Consider competing candidates in development, too.

8. ADOPT A COMBINATION STRATEGY

Evaluating ADCs in combination with other chemotherapeutic or targeted agents may give a better chance of improving efficacy and demonstrating clinically meaningful benefits for patients. An increasing number of ADCs are being evaluated in combination with immune checkpoint inhibitors. But beware of developing a combination product that payers will baulk at.

9. GO BEYOND CANCER

More than 98% of ADC candidates are being evaluated in oncology. But there are other possibilities, including in immunology and inflammatory conditions. Non-oncology development is still in early phases, so there's plenty to play for.

10. MAKE SURE THE PRICE WORKS

You will need to perfect the balancing act between the price of your ADC and its efficacy over standard of care. Higher pricing could restrict patient access, so line up robust efficacy and cost analysis data in a real-world setting to help achieve favorable reimbursement.

Published online 23 September 2019

IPF Failure Sets Back Biogen's Diversification Efforts

MANDY JACKSON mandy.jackson@informausa.com

Biogen recently has been working to diversify its portfolio and reduce the risk level in its research and development pipeline, but BG00011 for idiopathic pulmonary fibrosis (IPF) will no longer contribute to those efforts now that the company has ended a Phase II study for the drug due to safety concerns.

Pressure is building for Biogen to produce a higher number of R&D wins than losses after the company's big bets on Alzheimer's disease have failed, including the amyloid-targeting antibody aducanumab in March and the BACE inhibitor elenbecestat this month. The company quietly disclosed the end of the Phase II study for BG00011 in IPF on 16 September – three days after it and partner Eisai Co. Ltd. revealed the end of their Phase III program for elenbecestat.

Biogen updated its clinicaltrials.gov listing for the mid-stage BG00011 clinical trial, noting that the "study was stopped because of safety concerns. End-of-study and safety follow-up visits are in progress."

BG00011, which targets integrin alpha-V beta-6, originally was developed by Biogen before the drug was out-licensed to the start-up Stromedix Inc. The big biotech later acquired Stromedix in 2012 for $75m up front and up to $487.5m in milestone payments as the smaller firm was beginning Phase II development for the drug. *(Also see " 'Welcome home': Stromedix buy brings fibrosis drug back to Biogen " - Scrip, 16 Feb, 2012.)*

Scrip asked Biogen if the discontinuation of the most recent study would be the end of all development for BG00011 and if the company would have to write down the value of its Stromedix purchase on its earnings as a result, but it declined to address those questions.

BG00011 was being tested to see if it could improve lung function in IPF

"Biogen determined that the benefit-risk profile of BG00011, a therapeutic candidate for IPF, no longer met the criteria to continue the clinical trial," the company said.

Phase IIa results for BG00011 presented at the American Thoracic Society meeting in May 2018 focused on safety, pharmacokinetics and biological activity, showing dose-dependent effects on targeted genes related to IPF, but pulmonary function test results were not disclosed. The Phase IIa data were used to justify initiation of a Phase IIb trial, despite findings that three patients treated at a higher dose had sustained respiratory declines in the earlier trial.

The placebo-controlled Phase IIb study was meant to enroll 290 patients, but only 109 were enrolled, according to clinicaltrials.gov. The primary endpoint was the rate

TURN TO PAGE 23

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, 13–19 SEPTEMBER 2019

Event Type	Lead Company/Partner	Drug Name	Indication	Comments	Change To LOA (%)	LOA (%)
Phase III Published Results	Strongbridge Biopharma plc	Recorlev (levoketoconazole)	Cushing's Syndrome	SONICS; The Lancet Diabetes & Endocrinology, online	0	62
Phase III Updated Results	Novartis AG/Genmab	ofatumumab	Multiple Sclerosis	ASCLEPIOS I, II; Met Primary Endpoints	0	58
Phase III Updated Results	Centrexion Therapeutics	CNTX-4975	Osteoarthritis	VICTORY-3; Pain Reduced	0	68
Phase II/III Updated Results	bluebird bio	Lenti-D, gene therapy	Adrenomyeloneuropathy	ALD-102, -103, Starbeam; Promising Results	0	64
Phase III Top-Line Results	Aclaris Therapeutics, Inc.	A-101	Common Warts	THWART-2; Met All Endpoints	3	70
Phase III Top-Line Results	Jiangsu Hansoh Pharma	PEX168	Diabetes, Type 2	302; Improved Glycemic Control	-	-
Phase III Top-Line Results	Novartis AG	Zolgensma (onasemnogene abeparvovec)	Spinal Muscular Atrophy	STR1VE; Signicant Therapeutic Benefit	0	100
Phase III Trial Initiation	Alnylam Pharmaceuticals, Inc.	Onpattro (patisiran)	Transthyretin Amyloid Cardiomyopathy	APOLLO-B; an iv RNAi Therapeutic	38	62

Source: Biomedtracker | Informa, 2019

CONTINUED FROM PAGE 21

of change in forced expiratory vital capacity at one year. In addition to safety observations, secondary endpoints included the time it took for patients to experience disease progression, first exacerbation, hospitalization, and lung transplant or death as well as various measures of lung function and performance in a six-minute walk test.

ANOTHER SETBACK, BUT OUTSIDE OF NEUROLOGY

For Biogen, discontinuation of the BG00011 Phase IIb trial marks yet another setback for the company's high-risk R&D pipeline, which is focused largely on neurological diseases, including Alzheimer's programs, next-generation treatments in the company's keystone therapeutic area of multiple sclerosis (MS), and neuromuscular diseases.

However, investors aren't attributing a lot of value to the program. Biogen's stock price declined only 0.2% to $236.12 per share on 16 September as the change to its clinicaltrials.gov listing for BG00011 came to light later in the day. Biogen's stock opened lower at $234.86 on 17 September, but closed the day up 1.1% at $238.70.

BG00011 was a candidate that could have helped the company diversify its portfolio with assets that offset the high risk of its neuroscience-heavy portfolio, which Biogen has been under pressure to do, especially since the failure of closely-watch aducanumab. Company executives stressed during Biogen's second quarter earnings call that while neuroscience remains the top priority, diversification is top of mind as well, including through business development activities.

CEO Michel Vounatsos said during the call that Biogen is "refining the five strategic priorities we outlined two years ago. Our overarching goals are: to enhance our focus on our current commercial business; accelerate the areas with the most attractive opportunities to build new franchises; rebalance the risk/reward profile of our pipeline; prioritize our investment based on clinical data; and widen our lens to new therapeutic areas."

Those new therapeutic areas will include immunology, such as the BDCA2-targeting monoclonal antibody BIIB059 in Phase II for cutaneous and systemic lupus erythematosus (CLE and SLE). Also, Biogen and partner UCB SA plan to move the CD40 inhibitor dapirolizumab pegol into Phase III during the first half of 2020.

Executive vice president and R&D head Michael Ehlers noted during the company's second quarter call that Biogen has added 17 clinical programs to its pipeline during the last two and a half years. The company anticipates 10 mid- and late-stage clinical trial readouts during the next 18 months, including BIIB059 and head-to-head data for Vumerity (diroximel fumarate) in MS versus the company's own blockbuster Tecfidera (dimethyl fumarate), which will lose patent protection in 2020.

"As we widen our strategic lens, we will continue to mitigate risk by seeking later-stage assets, prioritizing targets that have been validated by human genetics, deploying biomarkers in early-stage clinical programs, and leveraging our asymmetric capabilities and expertise in neuroscience," Ehlers said.

Published online 17 September 2019

APPOINTMENTS

Executive	To Company	New Role	From Company	Previous Role	Effective Date
Neil McFarlane	Adamas Pharmaceuticals Inc	Chief Executive Officer and Director	Retrophin	Chief Operating Officer	16-Sep-19
Daniella Foster	Bayer AG	Head, Public Affairs and Sustainability, Consumer Health Division	Hilton Corp	Leader, Global Corporate Responsibility	16-Sep-19
Stewart Kay	Crescendo Biologics Ltd	Chief Business Officer	GlaxoSmithKline	Senior Director, Transactions	5-Sep-19
Aurelie Grienenberger	Eligo Bioscience	Chief Business Officer	Sanofi	Director, Transactions, Global Licensing and Business Development	17-Sep-19
Shubh Goel	Fennec Pharma	Chief Commercial Officer	Odonate Therapeutics	Vice President, Commercial Strategy and Operations	9-Sep-19
Jason Meyenburg	Gemini Therapeutics	Chief Executive Officer and Director	Orchard Therapeutics	Chief Commercial Officer	13-Sep-19
Elcin Barker Ergun	Menarini Group	Chief Executive Officer	Merck KGaA	Head, New Business	12-Sep-19

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

Source: Medtrack | Informa, 2019

DAMAGED?

Emirates SkyCargo

Never with us.

Concerned about the safety and integrity of your pharmaceutical cargo? Don't be. Emirates Pharma have you covered. We understand the importance of life-changing medicines, which is why we've developed an advanced transportation system specifically for temperature-sensitive pharmaceuticals. With state-of-the-art transit processes, cool chain facilities, quick transfers and a network of over 157 destinations across 6 continents, why would you risk shipping your precious cargo with anyone else?

skycargo.com/emiratespharma

Emirates Pharma