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Sanofi Ready To Pull The Plug On Regeneron 'Life Support'

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The lengthy antibody drug discovery collaboration between **Sanofi** and **Regeneron Pharmaceuticals Inc.** has been one of the industry's most productive partnerships, but it's poised to wind down at the end of the year, with implications for Sanofi's internal R&D.

Sanofi president-global R&D Elias Zerhouni said the time is right for the broad antibody collaboration to come to an end, largely because Sanofi now has the expertise it needs to discover antibody drugs internally. And, Sanofi also wants to prove to investors and others that Sanofi isn't dependent on Regeneron when it comes to R&D.

"There is always that sense out there that Regeneron is putting R&D [at] Sanofi on life

support," he said, speaking at a media event in New York City on Sept. 18. "It's not true."

The antibody drug discovery collaboration between the two companies has yielded three drug approvals from the FDA over the length of the agreement, two of them in the last year: the PCSK9 inhibitor *Praluent* (alirocumab), the interleukin-13/IL-4 blocker *Dupilixent* (dupilumab) for atopic dermatitis, and the IL-6 inhibitor *Kevzara* (sarilumab) for rheumatoid arthritis.

But Zerhouni pointed out that Sanofi has had many other drug approvals in the last five years. The company had 13 drugs approved since 2012, he said, and is on track to achieve the goal it set in 2014 to have 18 launches between 2012 and 2020.

"When I came to Sanofi, I realized that Sanofi R&D was not in favor of monoclonals," he said. "I believed that it was really important to partner and learn with a platform that was very efficient when we had zero internally."

"We could not generate our own antibodies. Today we can generate our own because it has been in a way commoditized."

Regeneron revealed during its second quarter financial release that the partnership would not be extended. Nonetheless, the two companies remain commercialization partners and are continuing to develop immuno-oncology drugs under a new alliance signed in July 2015 to collaborate on the discovery, development and commercialization of new antibody cancer treatments in IO, including a PD-1 inhibitor that is now in Phase II development.

"Because we had developed our own internal resources, I felt there was no reason to continue a generic agreement. What we felt was necessary was to accelerate our oncology programs," Zerhouni said.

Sanofi's and Regeneron's work together dates back to 2003, when Sanofi (then Aventis) took a stake in Regeneron and paid \$510m for rights to aflibercept for cancer, which was approved for colorectal cancer as *Zaltrap* but never gained significant commercial traction. The collaboration was reinforced in 2007, when the two signed a broader antibody drug collaboration. The partnership was supposed to run through 2012 but was later extended.

'DREAM' MOLECULES

Zerhouni talked about the experience with Regeneron at a presentation on the future of R&D at Sanofi. He spoke generally about the way Sanofi has changed its approach to R&D in the last five years by focusing on

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from the editor

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Diabetes drug makers have been hit particularly hard by downward pricing pressures.

Christopher Viehbacher lost his job running Sanofi in 2014, at least in part over his failure to get to grips with market pressures on the blockbuster insulin product Lantus. Novo Nordisk also saw the premature departure of CEO Lars Rebien Sørensen, at the end of 2016, following a very sticky patch in the US market and despite having won plaudits for his performance since taking on the role in 2000.

Sanofi is more diversified than Novo, and has many irons in the fire (see cover story), while Novo Nordisk is now looking to adjacent areas like obesity to kickstart new growth opportunities (see p4). Obesity has traditionally been a poisoned chalice for the pharma industry; it remains to be seen whether accessing it through

the diabetes door will yield better results. Meanwhile, both these makers of hugely lucrative insulin products have invested with mixed results in next-generation enhancements capable of sustaining once voluminous revenue flows in the face of both new product and bi-similar competition. Meanwhile, the wide range of products and constant incremental innovation for type 2 diabetes also makes for a space that is uncongenial to highly profitable pricing arrangements.

But looking at a broader landscape, downward price pressures may not be quite as powerful across US drug markets as some feared. President Trump has not taken the strong action he vowed against high drug prices, and AbbVie executives have apparently been telling investment analysts that by 2018 they may not be abiding by the price increase containment pledge they made in January.

Scrip

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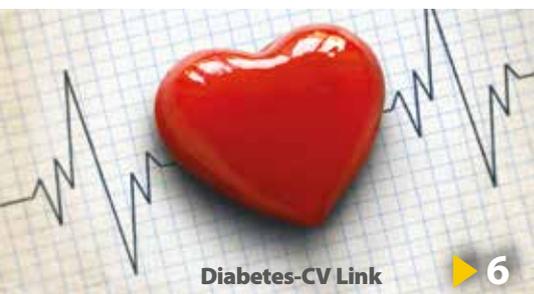
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Shanghai-based drug developer Zai Lab shares jumped on its first day of public trading, reflecting the strong interest in drug development in China.

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Refocused Novo Nordisk Says On 'Road To Recovery' After Traumatic 2016

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2016 was a bad year for **Novo Nordisk AS**; but the diabetes fighter learned from that tumultuous experience and is on the mend, according to the group's international operations chief Maziar Mike Doustdar.

In an interview with *Scrip*, Doustdar acknowledged that the Danish group could have reacted better to market events in 2016, but stressed that changes subsequently brought in by the company have put it on the road to recovery, and that the investment community has so far responded positively.

2016 CRASH

In the summer of 2016, the Danish group, pressed by rising price pressures and competition, was forced to slash its sales and profit forecasts, triggering steep slides in the Denmark-based company's share price, which in turn sparked lawsuits from aggrieved shareholders and prompted a restructuring within the company and changes in top management.

'For good reason, we lost some credibility last year with analysts, investors and shareholders. A couple of quarters of sticking to our agenda and our promises will be the best way to handle things going forward'

Doustdar, who spoke to *Scrip* on the sidelines of this year's European Association for the Study of Diabetes (EASD) in Lisbon, said that the drama had been painful, but that the company's response was already bearing fruit.

RECOVERY SEEN

"We previously had a value problem due to price problems in our largest market, the US. That can be understandable if you're a shareholder and bought Novo Nordisk shares at the beginning of 2016 and looked

at the shares' value at the end of that year and realized that the company lost some \$40bn in market capitalization; you would not be happy," he said. (Also see "Novo Nordisk Settles Over US Federal Investigation Of Marketing Practices" *Scrip*, 6 Sep, 2017.)

Since then, however, the tenor and focus of conversations with the investment community has improved.

"The atmosphere has changed a bit. Once again, we now talk about the science and what's about to come rather than defensively trying to convince listeners that the company has a sustainable strategy," he said.

He said the company will stay on message, stay transparent and focus on its 'niche' science abilities.

"For good reason, we lost some credibility last year with analysts, investors and shareholders. A couple of quarters of sticking to our agenda and our promises will be the best way to handle things going forward."

Doustdar said Novo Nordisk's US operations remain under pressure, but prospects for the rest of the world – which is

his business patch – look sturdy. "If you look at my part of the business, we grew some 5% during the first half which is very much in line with our targets and aligned with previous years."

"If you divide Novo Nordisk's commercial world into two halves and on one side you have North America and everything else is international operations, then while we've been challenged by pricing pressures in the US, driving down growth rates in North America from double digits to now low single digits [...] in all our other 194 markets –

which I represent – growth rates have been rock stable."

"We have historically been growing around 5% to 5.5%. In the first half of the year we have shown that once again and that reflects that the core of this company is very solid," he said.

He said the company's therapeutic focus on diabetes should help it stay on track and not get dangerously diverted.

"We have been able to stay focused on our patients more than some of our peers and that's in part because we don't try to do too many different things. The company was started by a founder who wanted to help his diabetic wife, so in a way the diabetes patient was our de facto first CEO," he explained.

That focus on the diabetes patient has kept Novo Nordisk from branching out into many other therapeutic areas – or engaging in significant M&A activity.

"Despite having good growth rates and having the cash to buy other companies that operate in other areas, we've instead tried to stay niche and stay focused, because when you do just one or two things, then hopefully you become very, very good at it," Doustdar said

"I have good knowledge about what a diabetic patient is but I would have no clue about oncology or respiratory or what have you so we at least like to think we understand this area quite well and that must stay with us as we go forward."

OBESITY MEETS DIABETES

Novo Nordisk aims to tap the synergies between diabetes and obesity.

"There are 400 million diabetics in the world and 600 million obese people in the world. Most of those 600 million are pre-diabetics. So, there is a direct connection between obesity and type 2 diabetes," said Doustdar.

One advantage would be using the same or similar molecules for treating both conditions.

"Broadening Novo Nordisk into the adjacent area of obesity is a better bet because we understand the customer, the patient,

the molecule. That makes more sense than getting tempted into trying to enter an area where we don't understand some of the core elements that are required for core success."

"Our current drug on the market for obesity is also a molecule we introduced for diabetes - liraglutide - so *Saxenda* and *Victoza* [respectively]. So we also know the molecule. The next generation obesity drug that we're bringing to the market is also based on a molecule that we're working on for diabetes - semaglutide. We also have a number of molecules that we won't use in obesity but at least for the foreseeable future the molecules are also somewhat connected. We have scientists who understand obesity from the molecule point of view," he explained.

"The other area of growing connectivity is evidence that diabetes might for some people be avoidable if they treat their obesity early enough. Especially type 2 diabetes, which is to a very large extent connected to obesity. If we can somehow reduce the BMI and the obesity for those who have not yet had a pancreas problem, maybe you'll also solve their diabetes. That kind of scientific knowledge will lead to better treatments and thereby help to prevent unnecessary death."

He said another field of research and commercial opportunity is the perceived inter-relationship between cardiovascular disease and hypoglycemia.

"Maybe we can finally start explaining to people that diabetes and living with diabetes and especially with 'hypos' [hypoglycemia episodes] relates to cardiovascular risks, which mean an earlier death or stroke."

"The connection between hypos and CV is extremely exciting ... The companies who get these things right - the ones who can take the science and commercialize it in the way that patients want - are the ones that are going to win," he added.

While Doustar believes type 1 diabetes can ultimately be cured, he thinks it will take much longer in the case of type 2 diabetes.

"There will probably be a cure found in our lifetime for type 1 diabetes ... but probably not for type 2 diabetes, because it's not a single disease. For type 2 diabetes, you need to solve and tackle the root causes, one of which is obesity." ▶

Published online 21 September 2017

Clustering Of Diabetes Subgroups May Aid Outcome Predicting

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Two decades ago cancer was categorized as one large disease pool. Today there are more than 200 known forms of cancer.

Could a similar evolution occur for identifying and treating various forms of type 2 diabetes?

Mads Krosgaard Thomsen, **Novo Nordisk AS's** chief science officer, thinks so - but he says the process will be less straightforward.

Much of the problem is genetic, Thomsen said when interviewed on the sidelines of this year's European Association for the Study of Diabetes (EASD) in Lisbon, Portugal.

"If you have cancer, a cancer genome analysis can tell you exactly what type of cancer you have and that can guide your therapy.

"But, within diabetes it's much more complex because there are more than 100 genes that make you susceptible to diabetes. So, that's not necessarily the right way to define subgroups of diabetes," he said.

TIERS OUTDATED

The current classification of diabetes into two main forms, type 1 and type 2, has been used for the past 20 years to delineate type 1 diabetes as an insulin-deficient form that needs insulin therapy.

But the approach has been less useful for breaking down the heterogeneity of type 2 diabetes. Still, there have been few attempts made to explore that heterogeneity - until now.

Novo Nordisk is taking part in research along with a number of Nordic entities, studying the viability of dissecting the heterogeneity of type 2 diabetes.

The hope is that by formulating a refined classification of the disease, scientists could offer ways to identify people most at risk of complications at the earliest stage of diagnosis, and then tailor the best treatment for each individual.

EASD ABSTRACT

In their study, the abstract for which was presented at EASD, the authors identified five replicable 'clusters' of diabetes patients,

with significantly different patient characteristics and risk of diabetic complications. The authors concluded that when taken together, it showed that "this new clustering is superior in terms of prediction of disease progression, particularly development of diabetic complications compared to the classical diabetes classification.

"Importantly, this prediction can be made already at diagnosis. In contrast to previous attempts to dissect the heterogeneity of diabetes, we have used variables reflecting key aspects of the diabetic disease that are monitored in patients. Thus, this clustering can easily be applied to both existing diabetes cohorts, such as from drug trials, and patients in the diabetes clinic," the authors said.

The heterogeneity of type 2 diabetes doesn't stem from a simple genetic linkage. "It is an inter-play of many things. So, I think we need to think more about the phenotypic [determined by both genetic makeup and environmental influences] classification of diabetes," Thomsen said.

Showing clear enthusiasm for the analysis behind the abstract, Novo's CSO told *Scrip* that "if we can break down various forms of type 2 diabetes and get it right based on relatively simple measures that every doctor can do, then we can identify what medication each individual patient needs for their situation." Opening a fresh vista on that disease through refined classification and therapy stratification has obvious commercial implications.

OBESITY CROSSOVER

Thomsen said the quest could eventually offer crossover insights into the linkage between obesity and type 2 diabetes.

"Even though the obesity science is still emerging, the factors behind obesity are even more heterogeneous than diabetes because it's quite clear that in obesity you have both the brain contribution - the fact that the eating behavior is both genetically and environmentally linked - and add to that the contribution by the individual's body composition," Thomsen said. ▶

Published online 19 September 2017

Diabetes-CV Disease Link Boosts EASD Buzz

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Rising evidence that severe low blood sugar levels raise the risk of type 2 diabetes patients dying from heart attacks and research into therapies addressing that link dominated this year's meeting of the European Association for the Study of Diabetes (EASD).

More than 15,000 delegates from over 130 countries attended the meeting in Lisbon, Portugal, where the scientific program included more than 1,200 talks and presentations on the latest results in diabetes research by leading experts in the field.

But delegates said the chief overall take-away from the five-day event, which ended Sept 15, was the rising evidence of the inter-relationship of cardiovascular disease (CV) and severe hypoglycemia.

"I've been to 25 EASD and 25 ADA (American Diabetes Association) meetings since 1993, and at long last we can declare victory and show that our research is improving heart outcomes. Diabetes is one of the top five killers in the world ... We can now start doing something about that," said Mads Krosgaard Thomsen, **Novo Nordisk AS**'s chief science officer.

His company's head of international operations Maziar Mike Doustdar summarized by saying that "what's happening more and more at these meetings like EASD and ADA is that we see cardiometabolic syndromes are more and more interlinked. It's almost hard to find a patient today who is taking insulin but who is not taking a lipid-lowering statin, or a hypertension drug. Or who has not been to a cardiologist once a year – or is also obese, if they have type 2 diabetes."

NOVO NORDISK'S DEVOTE

Doustdar and Thomsen spoke separately to *Scrip* at the annual EASD gathering as the Danish diabetes drug maker released new analyses from its DEVOTE trial, showing that people with type 2 diabetes who experience severe hypoglycemia are at greater risk of death. DEVOTE showed Novo Nordisk's *Tresiba* (insulin degludec) reduced the rate of severe hypoglycemia by 40% and the rate of nocturnal severe hypoglycemia by 53% compared to insulin glargine U100 in people with type



'Individuals who have experienced more hypos through their life will also experience faster heart attacks. This should help create more awareness of diabetes and its dangers'

2 diabetes. CSO Thomsen told *Scrip* the DEVOTE trial means that "now we can start linking the risk of dying in the next fortnight if you've had severe hypoglycemia. What is that risk? According to DEVOTE, it's 12 times higher than if you have not had that happen to you. And if the time frame is within one year, then the risk is three times higher that you'll die than if you didn't have an episode within that time. This doesn't say that we're proving that severe hypo precipitates death or cardiovascular attacks, but there's certainly a link," Thomsen said in an interview.

TAKING HEART AT EASD

Commenting on the increased CV focus in the field, Elisabeth Björk, who heads **AstraZeneca PLC**'s cardiovascular and metabolic diseases (CVMD) development unit, said: "for many years, diabetes research and clinical practice around diabetes has been very glucose-centric. It's been focusing on glucose and HbA1c and what its importance is and the differ-

ent treatments around that. The movement right now is towards analyzing what the impact is on the cardiovascular and renal part and the interconnection between the diabetes perceived and the kidney and the heart."

The field of diabetes therapeutics is now involving data in research about cardiovascular effects of different drugs and different drug classes that don't just address the glucose part of the HbA1c but also the effects of cardiovascular mortality and renal health. "That is why you're not only seeing endocrinologists and physicians in that field here at EASD but also more cardiologists and renal experts. They are all working together, while putting the patients in the center to try and piece together a total picture," she told *Scrip*.

Ludovic Helfgott, AstraZeneca's global vice-president for the CVMD business, told *Scrip* the diabetes research community "has now an added layer of scientific focus, that being cardiovascular benefits."

AstraZeneca used the EASD congress to release full results of its EXSCEL (EXenatide Study of Cardiovascular Event Lowering) trial. It showed cardiovascular safety with *Bydureon* (exenatide extended-release) in patients with type 2 diabetes at a wide range of CV risk.

“What we have done with the EXSCEL study – the biggest ever done with a GLP-1 analog therapy with 14,500 patients taking part – is we’ve proved that once-weekly exenatide is truly safe from a cardiovascular perspective in a broad patient population,” said Björk.

There were also fewer CV events observed in the exenatide arm of the EXSCEL trial, with 839 or 11.4% observed versus 905, equating to 12.2%, although the primary efficacy objective of a superior reduction in a composite measure of major adverse CV events (MACE) narrowly missed statistical significance ($p=0.061$). Headline results from the

six-year trial were released in May. Also, patients on exenatide had a 14% lower incidence of death than those in the placebo arm, she noted.

CV RISK MAY BOOST DIABETES AWARENESS

Novo Nordisk’s Doustdar said diabetic patients have hitherto not fully appreciated the urgency to treat their condition consistently. The related association of cardiovascular disease may help change that, to the benefit of diabetic patients. He used multiple sclerosis as an example.

“MS, like type 1 diabetes, is an autoimmune disease. When people discover they have it, they know it won’t kill them immediately but it can put them in a wheelchair, there’s a chance of losing your balance, or your speech, and so on. The fear of that means the patient runs to the doctor as soon as they have seen the first symptoms of MS ... compare that to the reaction of

type 2 diabetes patients. We have long shown that type 2 diabetes can end up with amputations, kidney failure, blindness before death earlier than planned, but still patients and doctors seem not to have shown the requisite urgency to get or give treatment.”

That will hopefully change now that more physicians are coming to the conclusion that severe hypoglycemia episodes result in cardiovascular risks. “So, individuals who have experienced more hypos through their life will also experience faster heart attacks. This should help create more awareness of diabetes and its dangers than we have previously been able to do.”

Summing up, Doustdar said that “if there’s one big theme that will change the diabetes landscape over the next decade, I think, it is the special connectivity between CV and type 2 diabetes.” ▶

Published online 15 September 2017

Teva Offloads Women’s Health Business To Two Firms For \$1.38bn

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Teva Pharmaceutical Industries Ltd. is making progress on its initiative to divest non-core assets to repay debt. The company said it will receive \$1.38bn from the sale of its global women’s health business to two different companies on Sept. 17, about a week after announcing an agreement to sell the IUD *Paragard* for \$1.1bn.

Most of the ex-US women’s health portfolio will go to the equity investment firm CVC Capital Partners, which agreed to buy Teva’s contraception, fertility, menopause and osteoporosis portfolio for \$703m. The portfolio includes more than 20 products, including *Ovaleap*, *Zoely*, *Seasonique* and *Actonel*, which generated \$258m in revenue in 2016. CVC said it plans to build on the women’s health care platform through further investments and acquisitions.

The over-the-counter (OTC) specialist **Foundation Consumer Healthcare** agreed to buy Teva’s emergency contraception portfolio, including *Plan B One-Step* and the other value brands *Take*

Action, *Aftera* and *Next Choice Dose* for \$675m. Combined annual sales of the products were \$140m in 2016.

Teva announced the deal to sell *Paragard*, along with a Buffalo-NY-based manufacturing facility, to **CooperSurgical Inc.** for \$1.1bn on Sept. 7. Together, the deals will help Teva put a significant dent in its multibillion-dollar debt pile. The company has vowed to put \$5bn toward paying down debt by the end of 2017.

The deals are subject to regulatory approval, but are expected to close before the end of the year, Teva said.

The divestitures have been in the works for several months under the direction of Teva’s interim CEO Yitzhak Peterburg. The company announced plans to divest its global women’s health business and European oncology and pain businesses in May as the company’s generic drug and specialty businesses have come under growing pressure. (Also see “*Teva To Divest Women’s Health, Some Oncology As CEO Search Proceeds*” *Scrip*, 11 May, 2017.)

Teva only announced the appointment of a permanent CEO on Sept. 11 after a seven-month search. (Also see “*Teva Lands A CEO: Can Schultz Replicate Lundbeck Success?*” *Scrip*, 11 Sep, 2017.) **Lundbeck Inc.** CEO Kare Schultz agreed to accept the job, which will require turning around the struggling generic drug leader.

“With the divestiture of Teva’s global women’s health products and the planned divestiture of the oncology and pain business in Europe, Teva is reinforcing its strategic focus on CNS and respiratory as its core global therapeutic areas of focus within Global Specialty Medicines,” the company said in a statement. “In these areas Teva maintains a strong pipeline and a portfolio globally, and will continue to invest in creating long-term value.”

Teva has a growing portfolio of branded central nervous system-focused drugs, though its top-selling specialty brand, *Copaxone* (glatiramer acetate) for multiple sclerosis, could face generic competition in the near-term for the important 40mg dose. ▶

Published online 18 September 2017

Pfizer Sets The Stage For A Biosimilar Showdown Over Exclusive Contracts

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Shutterstock, Alex Stanovetsev

A lawsuit filed by **Pfizer Inc.** against **Johnson & Johnson** over its defensive *Remicade* (infliximab) contracting will be a significant commercial test for the US biosimilar market. The lawsuit could have implications for how far brand manufacturers can go when it comes to protecting their blockbuster franchises through payer contracts, and whether or not biosimilars will have the chance to make substantial inroads in competitive markets.

Pfizer announced on Sept. 20 that it filed suit against J&J in the US District Court of Eastern Pennsylvania over what it calls anticompetitive practices that have denied patients access to its own version of infliximab, *Inflectra*, and undermined price competition in the emerging biosimilar market. J&J's exclusive contracting methods have effectively blocked *Inflectra* from accessing 70% of the commercial market, the lawsuit claims, even as Pfizer has offered to guarantee insurers it will offer *Inflectra* at a lower price versus *Remicade*.

The case could be groundbreaking in that *Inflectra* is a test for how the US biosimilar market might unfold in the near-term. The biosimilar, developed by **Celtrion Inc.**, is the first copycat version of a widely used and expensive monoclonal antibody to launch in the US. Pfizer launched *Inflectra* in the US in November 2016. Yet, despite payer enthusiasm for biosimilars that could lower the cost of popular biologics, Pfizer has struggled to secure reimbursement for *Inflectra* from commercial payers.

The issue, as Pfizer previously outlined in its second quarter earnings call, is that J&J has been able to monopolize the market through exclusive contracting, offering both steep discounts and bundling other portfolio products into contract negotiations. Indeed, J&J hasn't been keeping its initiatives under wraps and has been talking about the moderate impact of the *Inflectra* launch on *Remicade* thus far.

As Pfizer points out in the lawsuit, the risk is that J&J's strategy could have long-lasting impact. J&J's "biosimilar readiness plan" – as J&J calls it – is poised to "become the playbook for biologic originator firms seeking to preserve their dominance in the face of biosimilar competition," Pfizer says.

The insurer and the patient are still getting the discount they hoped for either way, but the larger question is what it could mean for the long-term viability of the biosimilar market and what role insurers should play in fostering the market at this early stage. It's also not clear what would happen if insurers refused to accept the exclusive contracts – would J&J really hold back on millions of dollars in rebates and discounts at a time when the pharmaceutical industry is facing growing public backlash over high drug prices, and the industry's reputation appears increasingly in question?

Despite calls from some in the industry that it might be time for drug manufacturers to do better when it comes to accepting the end of a drug's exclusivity period as part of a social responsibility strategy, recent actions by some players – **Allergan PLC's** deal with a Native American tribe over *Restasis* comes to mind – show the industry is continuing to pull out all the stops to protect its most valuable franchises.

At the heart of Pfizer's lawsuit is a claim that J&J required insurers to sign contracts explicitly agreeing not to cover *Inflectra*, either at all or only in rare circumstances when patients fail treatment with *Remicade* first. Fail-first is just as exclusionary, Pfizer says, because doctors would not prescribe what is essentially the same product to patients who fail treatment with *Remicade*, but would prescribe a different product instead.

"A key to J&J's ability to coerce insurers into accepting its exclusionary commitments is its denial of rebates to insurers that decline J&J's exclusivity commitments, thereby imposing a substantial financial penalty," the suit says. "In effect, J&J says to insurers, 'If you want to receive attractive rebates on *Remicade* for all of your existing *Remicade* patients' – rebates which, for some insurers, run into the tens of millions of dollars annually – you must agree to not reimburse for *Inflectra*, or to do so in the most limited of circumstances."

Insurers that decline J&J's offer face a substantial financial penalty, while those that do accept it receive what amounts to a multimillion dollar "payoff," according to the lawsuit. The tactics work largely because J&J has such a large stable of patients already on *Remicade*, which insurers need to cover, while Pfizer's rebates would initially be serving a much smaller group of patients, those who are new to treatment. Pfizer would have to price *Inflectra* below its own average variable cost to make up the lost J&J rebates and discounts.

Remicade presents specific challenges as well because it is administered through an infusion, which means providers must stock the product and pay for it upfront, relying on reimbursement from insurers to recoup the expense. Reimbursement challenges have left payers unwilling to stock *Inflectra*, which has trickled over to the government side of the business, even though Pfizer has secured better reimbursement under government contracts.

As of Sept. 1, about 90% of healthcare provider accounts using infliximab had not purchased any *Inflectra*, according to Pfizer. Additionally, *Inflectra* has secured less than 4% of total infliximab unit sales in the US as of Sept. 1. "Given the cost of biologic drugs generally, and *Remicade* in particular, there is almost no chance that providers will

pay for a product that is not widely covered by insurers for fear of stocking a product that will not be reimbursed after the provider administers it to a patient," the lawsuit maintains.

Remicade is priced at a wholesale acquisition cost of \$4,000 per dose, or \$26,000 per year, though J&J offers payers undisclosed rebates and discounts that reduce the costs substantially. Pfizer launched Inflectra at a 15% discount to Remicade, before undisclosed rebates and discounts.

J&J is also bundling rebates on different products in its portfolio along with Remicade, so that payers that don't accept exclusive contracts would also lose out on other portfolio rebates, according to the lawsuit.

INSURERS COWER UNDER THE PRESSURE

"Insurers have made it clear to Pfizer that its net cost for Inflectra would need to be low enough to offset the loss of J&J rebates," the lawsuit says. "Insurers have stated a desire to support biosimilars – and the lower per-unit prices they bring – but realistically cannot do so without incurring a substantial financial penalty imposed by J&J."

The lawsuit cites specific insurers, including the nation's largest, who have agreed to exclusive or fail-first contracts for Remicade, including **United Healthcare Services Inc., Anthem Inc., Aetna Inc.** and **Cigna Corp.**

In the case of United Healthcare, the health insurer had published a medical policy update classifying Inflectra at parity to Remicade initially but then changed course weeks later, according to Pfizer.

Pfizer also accuses J&J of promoting the fail-first policies put in place by insurers even though there is no medical reason for them. The lawsuit includes a sample from a J&J brochure touting, "Remicade (infliximab) is preferred over Inflectra (infliximab-dyyb) at United Healthcare." Pfizer insists tactics like the ones employed by J&J pose a risk to the entire biosimilar market, because drug manufacturers will not invest in developing the products if new entrants aren't able to break the "rebate trap" and generate a profit.

Pfizer is asking the court to declare J&J's conduct unlawful and in violation of the Biologics Price Competition and Innovation Act (BPCIA), and is requesting injunctive relief barring J&J from continuing to undertake exclusionary contracts, as well as monetary damages. ▶

Published online 21 September 2017

Pharma Executives Need Convincing About Value-Based Contracts

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Value-based contracts in the US – the linking of a drug's price to clinical or economic performance in the "real world" – may be viewed as a way to combat widespread concerns about high drug prices, but less than 50% of pharmaceutical company executives who took part in a recent survey have participated in them, or believe they are worth the economic risk.

Value-based contracts can expand patient access to new therapies, benefiting pharmaceutical companies, and limiting payers' financial risk, and can also lead to new commercialization approaches in global markets, notes a recent white paper from the consultancy PwC, whose Health Research Institute surveyed 101 pharmaceutical company executives and 100 health insurance executives on the issue.

But despite agreeing that value-based contracts could improve patient outcomes and reward pharmaceutical companies, only around 38% of pharmaceutical executives polled believed the potential rewards of value-based contracts are worth the risks, the report found (*Launching into Value: Pharma's quest to align drug prices with outcomes*).

That said, value-based contracts are very much in the news, with **Novartis AG** saying it was considering such an approach for its recently approved and high-priced CAR-T breakthrough therapy, *Kymriah* (tisagenlecleucel).

Other companies have also been active in this area – **Amgen Inc.** recently reported that it had entered into 75 value-based contracts.

LIMITED EXPERIENCE

Only around 25% of pharmaceutical executives polled have experienced their company taking part in value-based contracts, although among those that have participated in value-based contracts, 80% said the process was successful, the PwC paper reports. 92% of these pharma executives said they were somewhat or very likely to renew current value-based contracts. The contracts involved medicines in a range of therapeutic

areas, although most were concentrated in competitive, high-cost sectors, such as oncology, rheumatoid arthritis and cardiovascular disease. Around 34% of contracts were set up before regulatory approval, 28% at launch, and 18% later in a product's life cycle, at least one year after launch.

The PwC survey found 71% of pharma executives surveyed agreed that value-based contracts were a win/win opportunity, improving patient outcomes and rewarding companies for bringing innovative products to the market. However, pharmacy benefit managers (PBMs) and health insurer executives had a more mixed response to the process. All five of the largest US health insurers have participated in at least one value-based contract, and several survey participants from the sector expressed doubts about whether the contracts delivered additional value.

Barriers to the adoption of value-based contracts include fears about contravening anti-kickback regulations, and having to supply drugs under Medicaid at a price equal to the best available commercial discount, the report noted.

There also has to be agreement between companies and insurers about what drug performance metrics should be used. Around a third of pharma executives surveyed said that forging such an agreement was the most significant operational hurdle to be overcome. Indeed, only around 10% of payers strongly agreed, and 15% somewhat agreed, with the suggestion that their organization would benefit from a data sharing partnership with companies.

Could the Trump administration have an impact on value-based contracts? Around 31% of pharma company executives believed the administration is likely to accelerate the shift from volume-based payments to value-based payments, and 45% of pharma company participants said the administration was likely to accelerate the downward pressure on drug prices. Still, the industry was split on whether companies should limit drug price increases in the next fiscal year – 44% of those surveyed said yes, and 44% said no. ▶

Published online 21 September 2017

Applying Disruptive Innovation In CNS Clinical Trials To Reduce Variability



Research suggests that CNS drugs are 45% less likely to progress from Phase III to regulatory filing than other non-CNS drugs (*ref. Nat-Rev-Drug Discovery 14, 2015*).

The unmet medical need in psychiatry and neurodegenerative diseases is high in health care stakes where nearly 100 million Americans suffer from nervous system disorders, 2014 estimates from the Society for Neuroscience showed. In disease areas, such as Alzheimer's, there have been no new drugs on the market for the past 15 years.

What is impacting the availability of new drugs in the CNS space?

One major issue is the scales and outcome assessments that are used to derive the primary and key secondary endpoints in most CNS indications such as Alzheimer's, depression, schizophrenia. These scales – such as ADAS-Cog in Alzheimer's, HAM-D in MDD or PANSS in schizophrenia – were developed and validated more than two decades ago and are still considered as gold standard, but their ability to be sufficiently sensitive and specific to meaningful clinical change is coming under increasing scrutiny.

The insufficient robustness of the clinical endpoints compounded by their subjective nature is partly due to the difficulties patients encounter to reliably complete the existing tools, such as cognitive issues, recall, impact of co-morbidity disorders, and willingness to please the rater.

As expectations from regulatory agencies increase, the sole reliance on scales which are not sufficiently robust, sensitive or consistent is causing considerable difficulties for the drug development industry and the patients and families who are in desperate need of new medications.

This major issue is catalyzing the assessment of alternative outcomes and the interest in low burden wearable devices and sensors. That's because such wearables are capable of capturing clinically-relevant objective data which may be more sensitive to change than traditional scales in both clinical studies and the delivery of general healthcare solutions going forward.

The need for change is seen in analyses of past CNS clinical trials, particularly in the area of pain, such as in the 2014 FDA draft Guidance for Industry (*Ref: Analgesic Indications: Developing Drug and*

Biological Products; <http://bit.ly/2w6vUDf>) which said “there are known instances of failed clinical trials of analgesic drugs later found to be effective,” suggesting that some therapies may have failed despite being highly promising assets.

The lack of homogeneity among patient population is sparking an interest in the use of this technology to generate “digital” biomarkers. Researchers have shown the potential value in this data to identify more homogenous responders and have already developed specific algorithms and used activity and sleep data to identify specific cohorts that are more responsive to therapeutic intervention.

That testing vulnerability is amplified in the current drug development environment where mantras in the interest of efficiency and cost control prevail that call for clinical trials to fail fast - and early. Still, it is not in anyone’s interest for a potentially efficacious and much needed drug, that is apparently failing, to be shelved just because the assessments used to validate it are inadequate.

Standardization Needed

Many primary endpoints in CNS clinical trials are generated by using scales and questionnaires which, by their nature, are subjective. Clinical Outcome Assessment tools (COA) are commonly used and involve clinicians making their judgements based on observations and patient responses either verbally or to questionnaires. But while these assessments are commonly used in clinical practice, they can be prone to inter- and intra-rater variability and thus work well when a clinic has the same clinician observing and monitoring them from initial diagnosis through to completion of the treatment course.

Most clinical trials, however, are multi-centred and involve many sites in various countries, each site assigning two to three raters per trial and, consequently, assessments are conducted by a high number of different clinicians. Despite raters training and certification on key instruments to minimize and control rating variability, this problem cannot be fully eliminated due to the above-mentioned reasons. That, in turn, has the potential to undermine the nature of the trial, which is looking to determine whether a candidate treatment is having a positive impact, as it introduces a random variable to the process.

In addition, the use of in-clinic assessments is a snapshot approach, assessing a patient on a single day’s performance, which may or may not be reflective of their responses during the periods between site visit. Similarly, the behavior of individual patients may also be affected by when and where they are monitored, and could be an effect of the journey to the site, or the timing of the visit rather than reflecting the efficacy of the therapeutic

agent. For example, a patient being monitored at home may demonstrate different reactions to when monitored during a visit to the clinician’s office.

Calling Objective Wearables

One potential solution may be to remove or reduce the subjectivity from the data by collection of objective data through various forms of wearables. Wearable technology is already well established in the wellness space in the form of Fitbits, Moovs, Garmin and Withings for monitoring activity levels, heart rates and sleeping patterns. Medical grade versions of these consumer devices have been used by the research community for over 40 years and are well validated against gold standard technology. These initially were marketed to the “concerned healthy” wanting to track their ongoing health, fitness and wellness. Changes in sleep and activity levels can have a profound impact on dementia and so these devices are increasingly ensuring the accurate measurement of patient behavior.

Wearables combined with apps as part of a clinical trial protocol can help raise compliance rates - reminding patients when to take the candidate drug being tested - and reduce dropout rates.

Moreover, the smartphones in most people’s hands are capable of tracking many useful physiological data. Smartphones commonly have accelerometers, gyroscopes and magnetometers. They can also record video and act as voice recorders. Their full potential as a tool to capture clinically relevant data is currently being explored, as for example through use of the Roche PD app.

The constant monitoring remotely - sometimes referred to as telemedicine or mHealth - can also reduce the need for hospital or clinic visits and is being actively investigated by the payer and health systems. This approach is currently under investigation by companies involved in drug development, and technology is being used to support the remote monitoring of patients in both virtual and or hybrid studies where the number of site visits are being reduced or eliminated completely. The success of this approach will depend on the individuals who have been recruited into the trial but it is hoped that use of wearables has the potential to support better patient retention by allowing the creation of more patient centric trials; reducing the need to travel to the site, collect the data passively without the need to further burden the patient and collecting real-life data that is more robust, objective and less subject to patient recall.

The data being transmitted is thus in response to something happening to the patient, rather than third-party observation; it’s not subjective - and should thus reduce variability, which has undermined assessments of many drugs, particularly in the Alzheimer’s space, but also in

other CNS indications.

In addition to better quality data it is felt that these devices deployed and used by individuals in their real life will have the ability to capture data as they engage in their normal daily activities. This data has the potential to develop new endpoints that are more meaningful to the patients. The issues of patient engagement and centrality are becoming increasingly important. The FDA has announced the inaugural meeting of the Patient Engagement Advisory Committee (PEAC), a group that will focus on challenges of clinical trial design, conduct, and reporting identified by patients initially this group will focus on medical device trials. Hopefully the aspect of burden and the use of passive monitoring will form part of the discussion.

And progress is being made. Researchers from Sage BioNetworks and the University of Rochester in 2016 published data from a mobile application-based mPower study piloting new approaches to monitoring key indicators of Parkinson Disease progression and diagnosis, conducted through an iPhone app interface, by supplementing traditional behavioural symptom measurements with novel metrics gleaned from sensor-rich mobile devices.

The mPower study interrogated aspects of movement disorder associated with Parkinson disease through surveys and frequent sensor-based recordings from participants with and without the condition. The mPower app makes the user do tasks, such as tapping the screen to assess physical symptoms and track mental ones. The study sought to learn more about Parkinson's Disease and to better track the progression of the condition. In particular, the researchers wanted to know whether it is possible to distinguish dyskinesia - the involuntary muscle movements usually associated with the condition - from normal movements.

Benefitting from large enrollment and repeated measurements on many individuals, the researchers suggested that the data may help establish baseline variability of real-world activity measurement collected via mobile phones, and ultimately may lead to quantification of the ebbs-and-flows of Parkinson symptoms. Significantly, app source code



**Wearables
are capable
of capturing
clinically-relevant
objective data
which may
be more sensitive
to change than
traditional scales.**

for these data collection modules are available through an open source license for use in studies of other conditions.

Ranks Of Techno Players Rising

Disruptive technology vendors aren't sitting on their hands waiting for that to happen, though. Many are already active in this space; Qualcomm and Validic for example have data integration hubs that will allow collection of data from different sensors and wearables. Apple are building a flexible ecosystem integrating sensors and devices from a number of different vendors that link to its smartwatch and its acquisition of Beddit and recent digital health deal with Nokia (Withings) provides the capability of capturing a number of clinically significant endpoints in a passive low burden manner. New and innovative devices and sensors are entering the market with increasing speed - it is now possible to capture a number of physiological parameters from a wristwatch.

Embrace, a wearable technology design company based in Boston, Mass., in the US and in Milan, Italy, has developed a wearable - which looks like a very fashionable smartwatch - it has been designed to predict when an epileptic might be about to have a Grand Mal seizure that is currently in clinical trials. Components include an accelerometer, a gyroscope, an electrodermal activity sensor that has the potential to measure the patient's stress and a peripheral temperature sensor that can send out phone notifications to caregivers when a seizure appears imminent. This has the potential to remotely capture data that would allow the quantification of significant events that may be sensitive to disease progression.

Miniaturization will play a role in the next generation of devices. One of the leading companies in this space is MC10 Inc. with their Biostamp. This device will allow access to raw kinematic and electrophysiological data and is one of the smallest wearable sensors of the market - feeding into the need to create technology capable of capturing meaningful data but which have low patient burden.

New ways of capturing brainwave activity offer potential for generating deeper, longer-term data that can then be used for analysis and hopefully

better tracking of drug efficacy. The development of small, easy-to-wear single or two channel EEG (electroencephalography) sensor technology is a case in point, offering an electrophysiological monitoring method to record electrical activity of the brain. EEG sensors are typically non-invasive, with the electrodes placed along the scalp, although invasive electrodes are sometimes used such as in electrocorticography.

Data Handling & Privacy Challenges

The emergence of wearables does create major challenges associated with the handling and analysis of the huge volume of data that will be generated. Determining how that might be most efficiently constructed will be key to progress. Unconnected silos are not seen as part of that solution. The future world of clinical trials could revolve around data integrators linked to analytics platforms where data would be integrated and then analyzed.

To achieve this evolution requires an international stakeholder partnership, but getting there will require catalysts and drivers, not least for such disruptive technology to interface with clinical trials. Pharma companies are therefore not only going to need to embrace device and wearable designers, they will also have to collaborate with companies capable of handling big data – so it's no surprise to see tech giants such as Intel, IBM, Oracle and Google are looking at this sector. The development of machine learning and artificial intelligence applications will also be needed.

It also presumes access to, and storage of, big data, and people accepting its impact on their privacy and lives. Life is a cost-benefit analysis, especially

in the realm of health. Protection of privacy is also an issue. But distinction between continuous data streams versus the snapshot that often happens in a clinic is a key consideration.

Another question is the business model that would make this evolution happen. And whether it would be demand-led or supply-led.

Patient Pressure

Patients will play a key role in this evolution.

Patients, patient advocates and patient groups will be much more demanding of the healthcare industry. Stakeholder groups are becoming much more knowledgeable by the day and the emergence of wearables and devices and the data they collect will be empowering. We have all seen what a smartphone health app can do: track sleep, heart rates and other vital signs. These data can be used to identify whether a medicine or a candidate drug is delivering desired clinical outcomes, notify when medical intervention is required and monitor responses to treatments.

The uptake of wearables and devices in the CNS clinical research space will vary depending on the indications, sleep and movement disorders looking most promising.

It is hoped that use of wearables and new technology platforms will supplement, and perhaps eventually replace the current battery of instruments that are not robust and only address specific symptoms with objective endpoints that are reflective of the real lives of individuals and are more responsive to change than the current methodologies.

Valerie Legrand, VP Project Management, CNS, ICON plc

Valerie holds a Pharm D. from the University of Lyon, France, as well as a Degree in Statistics applied to Medicine (Paris VI University) and an Inter University Degree in Clinical Drug Development (DIU-CLIM, University of Lyon). With more than 20 years' experience in clinical research, mostly in the project management function of the CRO industry, Valerie has managed and overseen client portfolios and development programs spanning from phase I to peri-approval studies, including large phase III programs in various CNS indications. Valerie joined ICON in November 2010 in the role of VP Project Management, CNS, Pain and Aging Disorders, striving for innovation in processes and trial outcomes.

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Marie is part of the multidisciplinary Innovation team at ICON plc. She is a key intrapreneur and has specific responsibility for developing solutions in the direct to patient paradigm. Her primary focus is on the use of wearables and sensors in clinical trials, with emphasis on the potential to monitor the physical behaviours of the digital patient. She is a published author and has spoken at a number of international conferences.

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Once-Trusted Investment Advisor Burrill Faces Criminal Fraud Charges

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Steven Burrill once was the go-to source for life science financing and dealmaking data, well known via his firm Burrill & Co. as a trusted advisor to the industry, but now he's facing federal criminal charges related to alleged investment fraud that was the subject of now-settled civil litigation.

Burrill and Marc Howard Berger have been indicted by a federal grand jury in San Francisco, with Burrill facing 26 counts of wire fraud and one count each of investment advisor fraud and tax evasion in what the Department of Justice (DoJ) described on Sept. 18 as "an alleged scheme to siphon money from an investment fund." Berger is charged with three counts of preparing false tax returns in which Burrill did not report income he received from the alleged scheme.

The 34-count indictment cites Burrill & Co.'s Burrill Life Sciences Capital Fund III LP, a \$283m life science investment fund, as the start of the alleged fraud. The indictment alleges that Burrill issued false and misleading letters soliciting capital contributions to the fund from its limited partners. Once that money was in hand, Burrill allegedly was responsible for the transfer of millions in management fees to his investment and advisory companies – fees on top of normal investment management fees associated with such funds.

At least one lawsuit filed against Burrill and his associates, outlining similar allegations by former employee Ann Hanham, was settled in 2015. Hanham claimed she was fired after she discovered inappropriate transfers of investors' money into Burrill's business accounts and reported the withdrawals to her superiors.

DoJ alleges that Burrill also filed false and fraudulent tax returns that understated his income by excluding the purportedly fraudulent investment management fees. Berger willfully assisted in the preparation and presentation of those three tax returns, the government claims.

DoJ is prosecuting its case against Burrill and Berger based on an investigation by the FBI and Internal Revenue Service with assistance from the Securities and Exchange Commission (SEC), which settled its own claims against Burrill in March 2016. He agreed to pay back nearly \$4.8m of the \$18m he allegedly stole from investors and paid a \$1m penalty to settle charges that he misappropriated the funds. The SEC also barred Burrill from the securities industry for life.

Burrill's initial court appearance under the DoJ indictment is scheduled for Oct. 2. If convicted, he could be sentenced to a statutory maximum sentence of 20 years in prison plus a fine of \$250,000 or twice the gross gain for each count of wire fraud; five years in prison and a fine of \$250,000 for investment advisor fraud; and five years in prison and a \$250,000 fine for tax evasion.

Berger was arrested and entered a not guilty plea in front of San Francisco Federal Magistrate Judge Sallie Kim on Sept. 18. He was arraigned and released after posting bail, but will appear before Judge Richard Seeborg on Oct. 3. Berger's charges come with a statutory maximum penalty of three years in prison, but additional terms of supervised release, fines and restitution are possible. ▶

Published online 21 September 2017

CONTINUED FROM COVER

fewer, higher quality assets and by working on antibodies rather than small molecule drugs. The R&D chief has been out front and center talking about the changing environment at Sanofi as the company's all important diabetes franchise, led by *Lantus*, has matured and come under commercial pressure.

Zerhouni said the company is focused on finding "dream" molecules that address multiple targets and can potentially treat more than one disease.

Dupixent is one example, because it targets multiple pathways and has potential in multiple diseases. While it was approved for atopic dermatitis earlier this year, Sanofi/Regeneron announced positive Phase III data in asthma in September. (*Also see "Sanofi and Regeneron Hit Asthma Phase III Endpoints With Dupixent" Scrip, 11 Sep, 2017.*) It is also in development for the treatment of nasal polyps.

Sanofi currently has 47 molecules and vaccines in clinical development, including 13 in late-stage development, and across seven core therapeutic areas: immuno-inflammation, multiple sclerosis & neurology, oncology, rare diseases, diabetes, cardiovascular & metabolism and vaccines & infectious disease. The 47 molecules in the clinic target 90 diseases, he said.

"If you look at the totality of what you do, you need to be better qualitatively in what you do, but you also need to execute better," he said.

That means relying more on digital technology to improve drug development, he said, pointing out that Sanofi has been able to bring its average drug development timeline down to 8.5 years from the industry average of 10.5 years. Still, Zerhouni acknowledged that even more improvements are needed.

"We have rebalanced the portfolio so that we rely on partnerships a lot initially," he said. When he joined Sanofi as head of R&D in 2011, the company had 165 molecules in clinical development. "The number one job I had to do was eliminate 100 of them," he said.

But what is the number one thing Sanofi is missing? "If I have one dream, [it is] how to predict the efficacy and safety of combinations," he said. "Do I have a systematic way of doing that? If I did, I would be in such better shape." ▶

Published online 19 September 2017

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JAK Inhibitors Have Dupixent In Their Sights For Atopic Dermatitis

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Janus kinase (JAK) inhibitors and their potential to compete with **Sanofi** and **Regeneron Pharmaceuticals Inc.**'s much-touted *Dupixent* (dupilumab) to treat atopic dermatitis took centre-stage at the recent European Academy of Dermatology and Venereology meeting in Geneva.

The congress in Switzerland saw yet more strong data presented on Dupixent, which some analysts have predicted could be a mega-blockbuster, helped by its potential as an asthma treatment. In March this year, the US FDA approved the interleukin-4/IL-13 inhibitor in adults with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies – Europe is expected to follow suit soon, given that the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion in July.

In Geneva, results from the Phase III CAFÉ study were presented, looking at Dupixent in combination with topical corticosteroids (TCS) as a treatment for patients who are inadequately controlled with or intolerant to the immunosuppressant cyclosporine A – the latter is approved in Europe and Japan for atopic dermatitis, the most common form of eczema, but not the US.

In the study, 59% of patients who received Dupixent weekly with TCS, and 63% who received the combo every two weeks achieved a 75% or greater improvement in the Eczema Area and Severity Index (EASI-75) score at 16 weeks, compared to 30% of those taking placebo with TCS.

Marjolein De Bruin-Weller at the University Medical Center in Utrecht, noted that Dupixent with TCS significantly improved overall measures of disease severity “including lesions, itch, quality of life measures and symptoms of anxiety and depression in these patients.” She added that the safety profile in CAFÉ was consistent with three previous positive Dupixent Phase III studies in moderate-to-severe atopic dermatitis.

So more good news for Dupixent which had sales of €26m in the second quarter following its US launch and Sanofi noted in July that there is great demand for the therapy as the first biological option in eczema. (Also see “Atopic Dermatitis Market Snapshot: The Next Multi-Billion Dollar Opportunity” *Scrip*, 20 Oct, 2016.)

Clearly Dupixent holds the advantage but there is competition coming through the pipeline. At EADV, **Eli Lilly & Co.** and partner **Incyte Corp.** unveiled data from a Phase II trial of baricitinib, their closely-watched JAK 1/2 inhibitor which showed that after 16 weeks, 61% of moderate-to-severe atopic dermatitis patients treated with 4 mg dose of baricitinib plus TCS achieved a 50% or greater reduction (EASI-50) in their overall disease severity, compared with only 37% on TCS alone.

The 2 mg dose of baricitinib failed to reach statistical significance on the EASI-50 scale at 16 weeks but Lilly, noting that the drug was able to achieve improvement in both itch and skin inflammation, plans to initiate a Phase III clinical program for atopic dermatitis later this year. Commenting on the results, Emma Guttman-Yassky at

Mount Sinai Medical Center in New York said it is also important to note that in this study, patients had to fail four weeks of supervised therapy with a mid-potency TCS before randomization, “selecting for a difficult to treat patient population.”

She added that the results suggest baricitinib may have the potential to become an oral treatment option, something which is perceived as an advantage over injected Dupixent. Ian Somaiya, an analyst at BMO Capital Markets, believes that the Phase II results “should translate into Phase III success, and while efficacy of competitor drugs may appear superior, TCS run-in times and less potent TCS in the baricitinib trial suggest they may not be.”

He expects to see an approval in 2022 and is forecasting peak sales of \$3.7bn in adult atopic dermatitis, similar to his estimates for Dupixent. The promising data in this field is a boost for Lilly and Incyte, given that the FDA rejected baricitinib in its principal indication of rheumatoid arthritis amid despite concerns about thromboembolic safety, though the firms plan to refile the drug earlier than expected by the end of January 2018 – it is already marketed for RA in Europe as *Olumiant*.

Also coming up on the rails in the atopic dermatitis space is another JAK inhibitor – **AbbVie Inc.**'s upadacitinib. Data released ahead of EADV from a Phase IIb trial showed that 50% of patients on the highest dose (30 mg) achieved a 90% or more disease improvement in skin lesions (EASI-90) by week 16, compared to 2% for those on placebo.

In addition, significant improvement was observed with respect to pruritus, with the patients on 30 mg upadacitinib experiencing 69% improvement in itch, compared to 10% for those receiving placebo. Phase III trials will begin next year.

Upadacitinib is seen as key to AbbVie's future prospects as it faces up to life to pending patent expiries on its autoimmune behemoth *Humira* (adalimumab). Phase III trials of upadacitinib in rheumatoid arthritis and psoriatic arthritis are ongoing and it is also being investigated for Crohn's disease, ulcerative colitis and ankylosing spondylitis. (Also see “AbbVie's New Generation JAK inhibitor Looks Good But CV Specter Looms” *Scrip*, 12 Sep, 2017.)

As to whether the JAK inhibitors will make significant in-roads into Dupixent's market share in atopic dermatitis, Datamonitor Healthcare analyst Christina Vasiliou is not convinced. With specific reference to the baricitinib study, she told *Scrip* that the EASI-50 results for the 2 mg dose, and the fact that both the 2 mg and 4 mg doses failed to outperform control in terms of EASI-75 “negatively impact baricitinib's clinical attractiveness.”

Vasiliou added that much will depend on Phase III efficacy data for baricitinib and upadacitinib and how they perform against cyclosporine. As for what advantage the JAK inhibitors will glean from being oral, she said they will be attractive for patients who want to delay initiating biologic therapy and those with milder disease who have not responded to topical therapy. ▶

Published online 19 September 2017

No Clear Winner in BMS, Exelixis/Ipsen First-line Renal Cancer Race

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The battle lines have been drawn between **Bristol-Myers Squibb Co.** and **Exelixis Inc.** and partner **Ipsen** after strong data presented at the recent European Society for Medical Oncology congress in Madrid on their respective first-line renal cell carcinoma therapies saw both being touted as potentially practice-changing.

First up, even before the doors opened at ESMO, top-line results from an interim analysis were unveiled by BMS from the CheckMate-214 Phase III trial looking at its PD-1 inhibitor *Opdivo* (nivolumab) and CTLA-4 inhibitor *Yervoy* (ipilimumab) in advanced renal cell cancer. The study was stopped early after data revealed improvements in overall survival versus the standard of care, **Pfizer Inc.'s Sunitent** (sunitinib) – the news went down well with investors, coming after an announcement in August that the trial did not reach statistical significance on one of its other co-primary endpoints, progression-free survival.

That announcement pushed BMS stock to a 52-week high and once the congress kicked off, the enthusiasm for CheckMate-214 continued. The combo reduced the risk of death by 37% versus Sunitent in intermediate- and poor-risk patients and also significantly improved overall survival in all randomized patients, reducing the risk of death by 32%.

Furthermore, *Opdivo* plus *Yervoy* demonstrated a 42% objective response rate in intermediate- and poor-risk patients, and 9.4% were complete responses. The side effect profile was also good, with grade 3/4 adverse events experienced by 46% of patients in the *Opdivo* 3 mg/kg plus *Yervoy* 1 mg/kg combination arm and 64% in the Sunitent arm.

Presenting the data, Bernard Escudier, of the Institut Gustave Roussy in Villejuif, France, said the safety and efficacy profile of *Opdivo* plus *Yervoy* meant that the combo should become the standard of care for patients with first-line metastatic renal cell cancer who have a very poor prognosis. Speaking at the second presidential symposium at ESMO, in answering his own question of whether the superiority of *Opdivo*/*Yervoy* over Sunitent represented a paradigm change, Escudier said “yes, sunitinib has never been defeated before”, adding that it was brave of BMS to choose the latter as a comparator.

He went on to stress his view that checkpoint inhibitor first-line treatment would be “a new standard of care with massive impact.” However, Escudier put the emphasis on the ‘a’, adding that “it’s not the final picture yet.”

It certainly is not. The CheckMate-214 update included an analysis, highlighted at the presidential symposium but not at an ESMO briefing, which suggests no PFS benefit in PD-L1 negative patients. Also, another exploratory analysis showed that favorable-risk patients actually achieved higher response rates and longer PFS with Sunitent versus the *Opdivo*/*Yervoy* combo.

This information suggests that a lot of the press coverage on CheckMate-214 may have jumped the gun in claiming that the combo will be practice-changing as some key opinion leaders (KOLs) had suggested. The issue was taken up in an investor event that took

place just after the presidential symposium hosted by Exelixis and Ipsen which was organized to focus on updated results from the Phase II CABOSUN trial looking at *Cabometyx* (cabozantinib) as frontline therapy for renal cell carcinoma.

The first half hour of the CABOSUN meeting saw a panel of KOLs give their views on CheckMate-214. Sumanta Pal, from City of Hope Cancer Center in Los Angeles, said that the study was a very important one, showing the overall survival benefit with the combo, as well as a benefit in response rates. However, he also acknowledged that there may be a selected benefit in patients who have high levels of PD-L1 expression.

CABOSUN SHINES AGAIN

Back to CABOSUN and lead investigator Toni Choueiri of the Dana-Farber Cancer Institute in Boston noted that in the updated analysis, *Cabometyx* demonstrated a 52% reduction in the rate of disease progression or death, while median PFS was 8.6 months versus 5.3 months for Sunitent. Saying that the drug would offer a new treatment option for physicians in the first line setting, he pointed out that CABOSUN included patients with intermediate or poor prognostic factors - a high rate of bone metastases, two or more sites of metastatic disease, ECOG 2 performance status (ambulatory and capable of all self care but unable to carry out any work activities) and lack of prior nephrectomy. “This patient population fares poorly and is in need of new therapies to better control their disease,” Choueiri added.

Analysts at Jefferies liked the look of the CABOSUN data, highlighting that the hazard ratio was much improved to 0.48 from the prior 0.66. They expect first-line approval for *Cabometyx* in Europe in the middle of 2018, and earlier in the US, while the *Opdivo*/*Yervoy* combo, already approved for second-line in renal cancer, has yet to be submitted to the regulatory authorities for first-line use.

As to which company ‘won,’ Choueiri would not be drawn, saying a comparison of the trials was hard given the different patient sets. “What we have is an embarrassment of riches” in renal cell carcinoma treatment, he claimed, and doctors will now face a conundrum as what to use as first-line therapy.

Other factors will come into play. Alex Lebeaut, chief scientific officer at Ipsen, told *Scip* that for many patients, oral treatment (ie *Cabometyx*) may be preferable to having to go to hospital for infusions. There is also the issue of cost, particularly in Europe, where the price of checkpoint inhibitors such as *Opdivo* is a much-discussed matter.

The Jefferies analysts believe that the strong initial launch of *Cabometyx* in Europe “bolsters confidence of rapid adoption for second-line renal cancer” and beyond. They forecast \$520m peak sales across all indications.

Following the excitement over CheckMate-214 and CABOSUN, there was also considerable enthusiasm at ESMO for a *Cabometyx*/*Opdivo*/*Yervoy* combo. A Phase III trial - CheckMate 9ER - was recently initiated in first-line renal cell carcinoma investigating the triple combo and *Cabometyx*/*Opdivo* versus Sunitent, with results likely in 2020-21. ▶

Published online 18 September 2017

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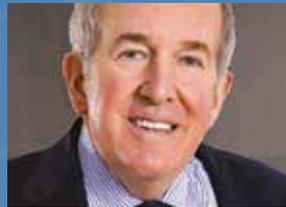
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Sanofi And NIH To Test 3-In-1 Antibody In HIV After Monkey Trial Success

STEN STOVALL sten.stovall@informa.com

Full protection against a monkey version of HIV has been reported using a tri-specific, genetically engineered antibody developed by **Sanofi** and US scientists – plans are now afoot to separately test the three-pronged therapy in healthy people and in patients living with HIV.

GENETIC ENGINEERING

Because naturally occurring HIV antibodies don't offer adequate protection against the virus, Sanofi and investigators from the National Institutes of Health (NIH) have turned to genetic engineering.

In their study, the three-in-one antibody protected monkeys from infection with two strains of SHIV, a monkey form of HIV, better than individual natural antibodies from which the engineered antibody is derived. It also stopped more HIV strains from infecting cells in the laboratory more potently than did natural, single antibodies. The study's results were reported in the journal *Science*.

The three HIV-binding segments of the antibody are based on three individual HIV antibodies, each of which powerfully neutralizes many strains of the virus.

Sanofi is manufacturing the tri-specific antibody for use in a Phase I clinical trial, which will be conducted by the National Institute of Allergy and Infectious Diseases, part of NIH, to test the antibody's safety and pharmacokinetics in healthy people, beginning in late 2018.

Talks also are under way with the NIAID-funded AIDS Clinical Trials Group to conduct a separate Phase I clinical trial of the antibody in people living with HIV.

But while promising, the study leaves much work still to be done to make an effective human treatment for HIV using the approach. The duration of the protection provided, for example, needs to

be determined. Datamonitor Healthcare analyst Michael Haydock thinks the tri-specific antibody concept is a smart way to capitalize on the promise of 'broadly neutralizing antibody' approaches.

"The obvious advantages to a tri-specific approach are that it broadens the scope of strains which could potentially be covered by the vaccine, and in terms of therapeutic treatment, it also provides a defense against resistance generation," Haydock told *Scrip*.

A high barrier to resistance is a major prerequisite for new treatments coming to the market because treatment guidelines currently recommend classes with high barriers to resistance – integrase and protease inhibitors – as preferred first-line agents, he noted.

MULTI-SPECIFIC ANTIBODIES

The research project is consistent with Sanofi's revamped R&D process which focuses on the exploration and development of multi-specific drugs.

Researchers at the NIAID Vaccine Research Center (VRC) and Sanofi tested dozens of bispecific and tri-specific antibodies to find the best-performing combination.

Individual antibodies were combined into tri-specific antibodies using technology proprietary to Sanofi. The most successful formula combines the unique structures of the broadly neutralizing HIV antibodies called VRC01, PGDM1400, and 10E8v4.

This "tri-specific" antibody used in the trial is a hybrid of those three antibodies, each of which targets a different vulnerable site on the virus. The engineered antibody grabs onto all three sites.

Datamonitor Healthcare's Haydock said that, if the engineered antibody was posi-

tioned as a prophylactic vaccine, there are two main commercial barriers it would face.

"Firstly, because it is a passive immunization approach – it doesn't actually stimulate immunological memory – it would have to be administered periodically, likely monthly or longer, to at-risk individuals and this could be costly in the long-term given it is a biologic. It would have a potential compliance advantage though compared to daily oral prophylactic regimens."

"Secondly, it would face competition from oral pre-exposure prophylactic regimens like **Gilead Sciences Inc.'s Truvada**, which will be genericized and much cheaper than an antibody by the time it reaches the market. Given that Truvada has already shown to be close to 100% effective in adherent gay and transgender individuals, I think it would be hard to demonstrate the added value of an expensive antibody, particularly in low-income areas like sub-Saharan Africa where prevention of transmission is most needed."

MAINTENANCE THERAPY

Haydock could envisage the antibody being positioned as a maintenance treatment once patients have achieved virologic suppression on current oral treatments.

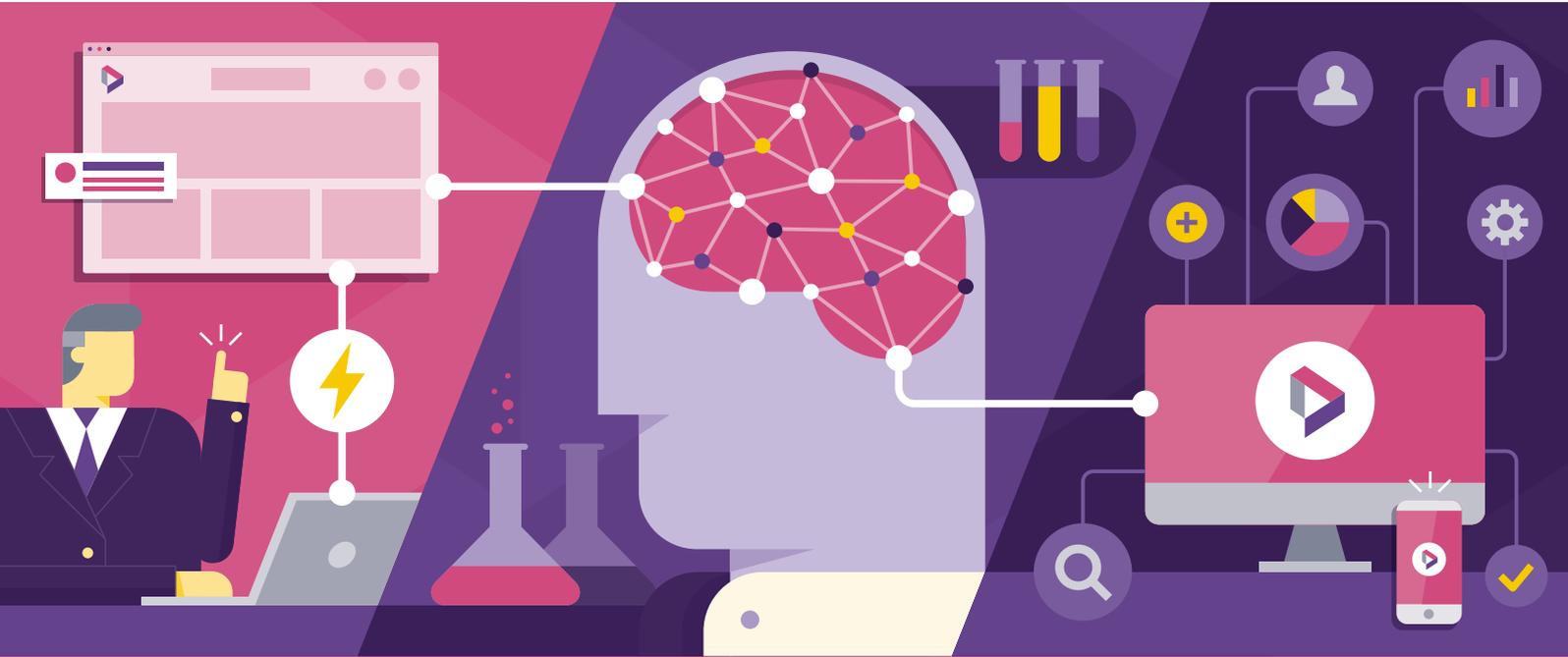
"Of course, it is too early to say if an antibody therapy alone would be as effective at suppressing the virus as a combination of oral antivirals with differing modes of action, but the advantages would be a potential improvement in compliance, as well as a potential tolerability improvement," he said in an interview.

Other infectious diseases, along with cancer and autoimmune diseases, could potentially be treatable with this tri-specific approach, the researchers said. ▶

Published online 21 September 2017

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Astellas Joins Search For Biomarkers, Drug Targets

MANDY JACKSON mandy.jackson@informausa.com

The treatment of psychiatric diseases, including schizophrenia and bipolar disorder, is anything but precise, but researchers hope biomarkers can help support the development of novel therapies and identify patients who will respond to new drugs.

Astellas Pharma Inc. is among the companies investing in psychiatric biomarkers. The company has a handful of schizophrenia drug candidates that it plans to move into the clinic within the next few years based on biomarkers that have been identified as potentially important. Astellas has an established presence in the field with *Seroquel* (quetiapine fumarate), which it licensed from **AstraZeneca PLC** to sell in Japan for several years before licensing the Japanese rights for the antipsychotic to **Kyowa Hakko Kirin Co. Ltd.** in February. Now, Astellas is looking to expand its portfolio in psychiatry – an area with significant unmet needs.

Scrip spoke with Gerard Marek, executive medical director for Astellas' global central nervous system (CNS) and pain drug development group, as well as Mickey Matsumoto, executive director and head of the CNS unit within the Japanese pharma firm's Candidate Discovery Science Labs, at the recent Precision Medicine Leaders Summit in San Diego.

The conference took place a few miles from the Astellas Research Institute of America (ARIA), which was established in San Diego in June as the company's global hub for neuroscience research. ARIA scientists are focused on the development of therapies that alleviate or lessen the burden of psychiatric disorders, including new treatment options for schizophrenic patients with psychosis and cognitive impairment, and bipolar disorder patients experiencing manic or depressive episodes.

Astellas has Phase I clinical trials under way for the internally developed oral small molecules ASP-4345 and ASP-6981, which have undisclosed mechanisms of action, for the treatment of cognitive impairment associated with schizophrenia. Matsumoto said the company has discovered drugs based on novel biomarkers in schizophrenia, but it will be another three or four years before those programs move into the clinic.

Matsumoto and Marek noted that the unmet need for new treatment options in psychiatry justifies Astellas' long-term investment in basic science and translational research.

BIG DATA EFFORTS UNDER WAY

Astellas and others are looking at postmortem brains for new biology and new drug targets related to psychiatric diseases, including schizophrenia and bipolar disorder. The company is one of many firms participating in the Lieber Institute for Brain Development's efforts to find new biological pathways and validate compounds for the treatment of psychiatric diseases.

Marek explained the goal is to find biological factors, imaging techniques or genetic signals that show in Phase I whether a novel drug is active in the brain, with the hope that those data translate to a signal of efficacy in Phase II clinical trials.

He said the company's two drugs now in Phase I to treat cognitive impairment in schizophrenia are based on accumulated knowl-

edge of what might help patients with memory, following instructions and maintaining focus. However, better genetic and other data could generate more effective treatments for cognitive impairment and negative symptoms – such as inability to think clearly and empathize, lack of motivation and social participation – even if just for certain subgroups of patients.

"We don't have a lot of biomarkers," Marek said. "We need a revolution." As in Alzheimer's disease, where treatment is shifting to earlier and earlier stages of the disease, including prodromal patients or those not showing symptoms, the revolution in schizophrenia may include a shift to prodromal patients if biomarkers or behavioral patterns related to progression of the disease can be identified. But without validated genetic or other markers for people who are likely to progress, Marek said it is difficult to ethically run clinical trials for prodromal schizophrenia.

Astellas has invested in its own research in these areas in addition to participating in larger initiatives like those at the Lieber Institute, because "the way we look at it, we don't really have the luxury of waiting for everything to be developed. Every day patients have psychotic breaks [but] advances in neuroscience are such that we're continuing to understand the brain better all the time."

TAPPING INTO ACADEMIC RESEARCH

During a panel at the conference about precision medicine approaches in psychiatry research, **University of California, San Francisco** (UCSF) psychiatry professor Daniel Mathalon said that unlike in Alzheimer's, where there's a lot of knowledge about the disease's pathology, the same kind of knowledge base doesn't exist in schizophrenia, where diagnosis relies on behavioral assessments.

However, Mathalon noted, there's growing agreement that the condition is actually several diseases. New clinical criteria have been able to predict that about 20% to 30% of patients will progress to psychosis, but more accurate predictors are needed.

"We need to be better than that in accuracy from the standpoint of just implementing existing treatments," he said. "Antipsychotic medications have a lot of deleterious side effects, and risks for long-term side effects, like involuntary movement disorders – things that we do not want to expose young people to if they do not need it. Knowing that someone's at 20% or 30% risk of transitioning to psychosis isn't enough of a justification for introducing antipsychotic medication."

He said many in the field are using electroencephalogram (EEG) tests and magnetic resonance imaging (MRI) to find and validate predictive biomarkers among high-risk patients, but EEG and MRI methods have not undergone rigorous testing to establish their validity. But, Mathalon added, "there's been a sense in the field that that kind of research is not easily funded and we should move ahead with our biomarkers even before we've really got a good grip on whether they have the properties of a biomarker that one would expect to need to have success." ▶

Published online 15 September 2017

Report: Women Eschew Life Science Companies That Lack Female Leadership

MANDY JACKSON mandy.jackson@informausa.com

It's a Catch 22: 46% of women surveyed about gender diversity in the life science industry said they would not accept a job at a company that had an all-male management teams and boards and where they were interviewed only by men. But how does an employer hire more female executives for leadership roles if those job offers are rejected due to a lack of women leaders?

The finding came from a report called "Opening the Path to a Diverse Future" released by the Massachusetts Biotechnology Council (MassBio) and the executive recruiting company Liftstream on Sept. 21. The report was informed by responses from 723 men and women as well as 70 companies to a detailed questionnaire about the gender gap in life science leadership roles, job recruitment and retention, compensation, career development and company culture. The goal was to identify reasons why women account for a smaller percentage of leadership roles even though the same number of men and women enter the industry; the report also recommends corrective actions.

Abbie Celniker, a partner at Third Rock Ventures and chair of MassBio's board of directors, predicted that one of the report's key findings – that almost half of women eschew executive roles at companies with male-dominated leaders – would be a surprise to both men and women working in the life science industry. However, she said in an interview with *Scrip* that she hopes it prompts women to take those jobs to help diversify those companies and change their corporate cultures.

"If women don't see a balance, I hope they'll be more motivated to take a risk and put themselves out there for those jobs," Celniker said.

DISPROVED ASSUMPTIONS

Liftstream CEO Karl Simpson said the report disproves a lot of assumptions about women in the life science workforce and shows that there are things companies can do to diversify at all levels.

"One assumption is that women are not forthcoming enough, that they don't put

Individuals Who Frequently Ask For Promotions

	CONTRIBUTOR	MANAGER	MID-LEVEL LEADER	FUNCTION LEADER
Women	37.8%	41.9%	41.2%	38.7%
Men	28.8%	33.3%	31.5%	12.5%

Source: "Opening the Path to a Diverse Future," MassBio and Liftstream

their hands up or don't have the confidence to ask for things that men are asking for, and their ambitions are not the same as men," Simpson told *Scrip*. "This dismantles those arguments in a pretty conclusive way. These long-held assumptions need to be looked at and we need to follow the evidence."

At all levels – contributor, manager, mid-level leader and function leader (vice presidents and senior vice presidents) – women asked for a promotion more frequently than the men who were surveyed.

One issue identified in the report as contributing to the imbalance of women and men in leadership positions is the way that companies hire for those roles, which largely relies on professional networks – networks that tend to be dominated by men.

"In the work we've done in looking at diversity on boards of directors, professional networks perpetuate the problem. They tend to be very much weighted to your own gender, by virtue of your social networks," Simpson said. "If you're operating at the C-level or the level below that, the statistical picture shows that many of your peers are going to be males. If you're looking within that [for new hires], you're going to generate more men than women. If that was substituted with a more meritocratic process, to bring in more men and women and evaluate them the same, you will have more women that merit the position."

MassBio and Liftstream recommend broader searches for new hires, extending beyond professional networks and utilizing outside sources to promote job openings.

Celniker also noted that the life science industry needs to do a better job of providing networking opportunities that bring men and women together rather than segregating them. Better networking com-

bined with a better understanding of women's experiences with hiring, recruitment, retention and promotions in the industry – as highlighted in the MassBio and Liftstream report – could go a long way to reducing the gender gap at middle and higher levels of company leadership, she said.

GREATER DIVERSITY, GREATER SUCCESS

And, various studies have shown, more diverse companies are more successful.

"We know we are running highly innovative companies and we know that innovation is supported by having diverse groups tackle problems," Celniker said. "MassBio is really concerned about workforce management for companies in the area, but you're not tapping a major part of the workforce to populate the executive leadership of these companies."

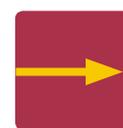
MassBio and Liftstream noted that while the women, men and companies surveyed for their report were all located in Massachusetts, since the region is one of the largest – if not, the largest – life science clusters in the US, the findings are reflective of the industry nationally.

Celniker stepped down from the CEO role at **Eleven Biotherapeutics Inc.** last year after it acquired **Viventia Bio Inc.** to shift its focus from ophthalmology to cancer. She became a partner at Third Rock to focus on new company formation as well as recruiting new talent. (*Also see "Viventia's Cancer Ambitions Go To Eleven" Scrip, 21 Sep, 2016.*)

"A couple of years ago, I was chair of a board of a small startup in California and I found that at venture-backed companies, there were only two female chairs reported. That was an eye-opener for me," Celniker said.

CONTINUED ON 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.



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Selected clinical trial developments for the week 15–21 September 2017

LEAD COMPANY/PARTNER	COMPOUND	INDICATION	COMMENTS
Updated Phase III Results			
La Jolla Pharmaceutical Co.	LJPC-501 (synthetic human angiotensin II)	hypotension/shock	ATHOS-3; survival benefit in patient subgroup.
Phase III Interim/Top-line Results			
Versartis Inc.	somavaratan (long-acting rhGH)	pediatric growth hormone deficiency	VELOCITY; missed primary endpoint of non-inferiority vs daily GH.
Nabriva Therapeutics AG	lefamulin, oral and iv	community-acquired pneumonia	LEAP 1; positive results.
Sanofi/Regeneron Pharmaceuticals Inc.	<i>Dupixent</i> (dupilumab)	atopic dermatitis, moderate-to-severe	LIBERTY AD CAFÉ; positive results.
Anylam Holding Co./Sanofi	patisiran	hereditary ATTR amyloidosis	APOLLO; RNAi primary and second endpoints.
GlaxoSmithKline PLC/Innoviva Inc.	<i>Trelegy Ellipta</i> (fluticasone/umeclidinium/vilanterol)	chronic obstructive pulmonary disease (COPD)	IMPACT; once-daily inhaler, exacerbations reduced vs Relvar/Breo Ellipta .
Shire PLC/Shionogi Ltd.	<i>Intuniv</i> (guanfacine)	adults with attention deficit hyperactivity disorder	Met primary endpoint, first study in adults.
AbbVie Inc./Roche	<i>Venclexta</i> (venetoclax) with rituximab	chronic lymphocytic leukemia	MURANO; positive results.
Novartis AG	<i>Xolair</i> (omalizumab)	chronic spontaneous urticaria	OPTIMA; well controlled symptoms after treatment interruption.
Phase III Initiated			
Janssen R&D LLC/MorphoSys AG	<i>Tremfya</i> (guselkumab)	psoriatic arthritis	A human anti-IL-23 MAb.
Phase III Announced			
Athenex Inc.	KX2-391	actinic keratosis	On the face or neck of adult patients.
Updated Phase II Results			
Bavarian Nordic AS	MVA-BN RSV vaccine	RSV infection	Durable immune responses.
Gemphire Therapeutics Inc.	gemcabene	dyslipidemia	COBALT-1; ROYAL-1; safe and effective in high-risk patients.
Prometic Life Sciences Inc.	PBI-4050	Alström syndrome	Sustained efficacy and safety.
MyoKardia Inc.	MYK-461 (mavacamten)	obstructive hypertrophic cardiomyopathy	PIONEER HCM; additional positive data.
Cytokinetics Inc./Amgen Inc.	omecamtiv mecarbil	congestive heart failure, ischemic and non-ischemic disease	COSMIC-HF; well tolerated, clinical benefits.
Genexine Inc.	GX-H9	short stature	Safe and well tolerated.
Janssen R&D LLC/MorphoSys AG	<i>Tremfya</i> (guselkumab)	psoriasis	VOYAGER-1; durable responses.

Source: Biomedtracker

CONTINUED FROM PAGE 21

“When I was a CEO and I would go to a leadership summit for the venture firms backing the company I was leading, there were a couple of times when I was the only woman when there were 30 or 40 people there,” she continued. “So, when I was trying to decide what to do after two CEO stints, I wanted to be innovative and be involved in establishing companies, but I also wanted to be involved in recruiting talent. At Third Rock, it was a great opportunity to influence that – to be a role model to recruit women into the companies we were starting as well as to the boards.”

PERCEPTION VERSUS REALITY

Celniker and Simpson both note that companies have to make a concerted effort to both establish gender diversity policies and follow through on those programs, since the MassBio and Liftstream report points out that employees, especially women, don't see those programs as uplifting women as much as the companies do. Only 9.2% of the women and 26.6% of men surveyed believed that their companies were fully inclusive, versus 39% of companies that responded to

Seven Broad Approaches To Improve Gender Diversity

1. Support women at all levels of employment, making sure they have equal access to career development, training and mentoring opportunities.
2. Provide new networking opportunities so that women and men are not segregated.
3. Share best practices between companies, so everyone understands what works, what doesn't and what can be improved.
4. Establish metrics of how many women and men should be in various company positions and continually assess progress.
5. Engage employees and colleagues in dialogue about gender diversity and encourage open discussion of the issue.
6. Establish a culture of inclusion that starts with company leadership and filters through all levels of a company.
7. Leadership should lead on this issue, setting standards for inclusion and enforcing them throughout the company.

Source: “Opening the Path to a Diverse Future,” MassBio and Liftstream

the survey. Both individuals and company representatives were invited to respond to the online survey. “Organizations need

to do more to find out what employees are looking for, what they want and what they need to be more engaged employees,” Simpson said. “If organizations offer no flexibility, but are trying their best to recruit women to join them, that may be what's holding them back.”

Having flexibility was important to both women and men, but more so for women. Of those surveyed, 37% of women said flexibility was important when they considered which companies to work for and 25% of men ranked flexibility as an important factor.

However, offering flexible work hours is just one thing out of many that companies can do to improve gender diversity. MassBio and Liftstream laid out seven broad approaches and 50 recommendations that the life science industry and its companies should consider (see box).

“I've been asked the one thing that companies should do, but one thing is not enough. There are many things companies should do,” Simpson said. “If organizations are looking for a silver bullet approach, I'm not so sure they're going to have success on this issue.” ▶

Published online 21 September 2017

APPOINTMENTS

Sosei Group Corp. has appointed **Chris Cargill** head of investor relations and corporate communications and **Kieran Johnson** group financial controller. Cargill joins the company from J.P. Morgan, where he was vice president in the UK healthcare investment banking and corporate broking group. Johnson was previously financial controller for GlaxoSmithKline's UK pharmaceutical and marketing division.

Matthew Hall has joined **Tusk Therapeutics** as chief financial officer, bringing over 20 years of corporate finance experience to the company. He previously was chief financial officer at Simbec-Orion Group.

Allied Minds has named **Harry Rein** independent non-executive director. Rein brings experience from the venture capital sector and most recently was general partner for 10 years at Foundation Medical Partners

(Foundation). Before this, he was founder and managing partner at Canaan Partners.

Aeterna Zentaris Inc. has appointed **Jeffrey Whitnell** interim chief financial officer – effective Sept. 25, 2017. Most recently, Whitnell was vice-president, finance & controller of Lifewatch Services Inc., and before that, he was chief financial officer and controller of Reliefband Medical Technologies. Whitnell also held various senior finance positions in various companies, including Ovation Pharmaceuticals, Medichem Life Sciences, Akzo Nobel and Motorola.

CTI BioPharma Corp. has named **Laurent Fischer** chair of the board. The company has also promoted **David Kirske** to chief financial officer (CFO) and **Bruce J. Seeley** to chief operating officer. Fischer has been director of the company since July and is senior vice president, head of the liver therapeutic area at Allergan. Kirske was previously principal financial and accounting

officer and before joining CTI, he was an independent CFO consultant. Prior to this promotion, Seeley was chief commercial and administrative officer at the company.

Jeff Ajer, executive vice president and chief commercial officer of BioMarin, has joined **Nektar Therapeutics'** board as an independent director. Ajer joined BioMarin back in 2005 and has held roles of increasing responsibility, including vice president commercial operations; senior vice president and chief commercial officer; and executive vice president and chief commercial officer. Before joining BioMarin, Ajer was vice president, global transplant operations at Genzyme Corporation.

Alma Bio Therapeutics, a company focused on auto-immune diseases, has appointed **Pierre A. Morgon** to its board. Morgon brings more than 30 years of life science industry and management experience to the company.

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