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Adcoms underwhelmed by abuse-deterrence of immediate-release opioid, call for higher bar

By Mari Serebrov, Regulatory Editor

The FDA's Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee gave the agency a lot to ponder as it considers whether to approve Mallinckrodt plc's new immediate-release (IR) formulation of oxycodone and determines if it warrants abuse-deterrent labeling.

The joint committees voted 10-7 Wednesday to recommend approving MNK-812 for the management

See Adcoms, page 3

'Using a dimmer-switch approach'

Cadent finds its rhythm in $40M series B for CNS disorders

By Marie Powers, News Editor

Self-described precision neuroscience company Cadent Therapeutics hauled in $40 million in a series B financing led by Cowen Healthcare Investments and Atlas Venture with participation from Qiming Venture Partners, Access Industries, Clal Biotechnology Industries, Novartis Institutes for Biomedical Research and Slater Technology Fund.

The round is designed to support the company's lead program, CAD-1883, a selective positive allosteric modulator of the small conductance calcium-activated potassium (SK) channel to treat essential tremor (ET) and spinocerebellar ataxia. The company has a phase I dose-escalation study of the oral small molecule underway in individuals with ataxia that has been well-tolerated at all doses with no adverse effects observed to date. By year-end, Cadent plans to initiate an open-label, non-randomized, single group assignment, interventional

See Cadent, page 4

EORTC-NCI-AACR 2018

'Threading the needle' with antibody-drug conjugates

By Cormac Sheridan, Staff Writer

DUBLIN – There are 98 antibody-drug conjugate (ADC) monotherapy development programs currently in the clinic, in addition to the four products already on the market, Steve Coats, vice president of R&D at the Medimmune arm of London-based Astrazeneca plc, told the audience at a workshop session on ADC warheads at the 30th annual EORTC-NCI-AACR meeting Wednesday. "They're probably not the magic bullets we had anticipated," he admitted. Nevertheless, interest in those agents remains high because of their ability to elicit responses in highly refractory cancer patients.

The vast majority of the programs he identified remain early stage – just six are in phase III, while another 16 are in phase II, with the remainder in phase I. The late-stage contenders include depatuxizumab mafodotin (ABT-414), which Abbvie Inc. is developing in glioblastoma with an endothelial growth factor receptor (EGFR) amplification. Immunogen Inc. is in phase III in platinum-resistant ovarian cancer with mirvetuximab soravtansine, which targets folate receptor alpha. Daiichi Sankyo Co. Ltd. is in a head-to-head phase III trial in HER2-positive breast cancer which pits its ADC DS-8201a against the approved drug Kadcyla (ado-trastuzumab emtansine).

Synthon Biopharmaceuticals BV is also in phase III in HER2-positive breast cancer with another HER2-targeting agent, [vic-]trastuzumab duocarmazine (SYD-985). Immunomedics Inc. is in phase III in

See EORTC, page 5

Newco News

Acquist highlights role for UA-targeting lead candidate against NASH

By Michael Fitzhugh, Staff Writer

SAN FRANCISCO – Acquist Therapeutics Inc., a Westfield, N.J.-based company targeting enzymes that regulate both production and excretion of uric acid (UA), reported that in human liver cells treated with a nonalcoholic steatohepatitis (NASH) promoter, its lead candidate, ACQT-1127, blocked a 70-fold increase in UA by more than 98 percent and reduced by more than half a marked increase in triglycerides. The candidate also brought dysregulated levels of seven NASH-related

See Acquist, page 6

Cellanyx reports live cell biopsy-on-a-chip data, works to fund prostate cancer trial

By Stacy Lawrence, Staff Writer

Distinguishing indolent cancer, which is unlikely to spread, from an aggressive tumor that will metastasize to different parts of the body remains a challenge in practice. That makes it easy to overtreat indolent cancer, which is thought to be common particularly among prostate and breast cancers.

Cellanyx LLC, a spinout from MIT and Columbia University, has developed its first-in-class Living Cell Phenotypic cancer diagnostic platform that's designed to offer individual cancer patient

See Cellanyx, page 7

Other news to note

Advanced Proteome Therapeutics Corp., of Vancouver, British Columbia, reported positive results from animal studies that were conducted in collaboration with **Heidelberg Pharma AG**, of Ladenburg, Germany. The lead antibody–drug conjugate (ADC) has demonstrated complete tumor regression at a single low dose in two challenging mouse models of human cancer (JIMT-1, NCI-N87) over extended observation periods with clear superiority over benchmark molecules used as positive controls. The potency and efficacy exhibited by the ADC is profound and the studies are still ongoing, as the improved condition of the test animals permitted a longer-term evaluation than originally contemplated, the companies said. They agreed to extend their collaboration and will continue to identify and test ADC drug candidates that best exploit the combined strengths of both their technologies, including APC's proprietary site-selective protein modification technology and Heidelberg Pharma's ATAC technology, featuring the mushroom toxin amanitin. Their research has led to conjugates that possess high target-specific cancer potency established in several human cancer cell types.

Alizé Pharma 3, of Lyon, France, said it is structuring its product portfolio in order to become a leading global rare disease company. Its first two assets are AZP-3601, a potential best-in-class parathyroid hormone (PTH) analogue designed for the treatment of hypoparathyroidism; and AZP-3404, a small peptide leveraging the biology of insulin-like growth factor binding protein-2 for the treatment of syndromes of severe insulin resistance and monogenic obesities.

Basilea Pharmaceutica Ltd., of Basel, Switzerland, said new preclinical data on its clinical-stage cancer drug candidate, BAL-101553, are being presented at the EORTC-NCI-AACR symposium on Molecular Targets and Cancer Therapeutics in Dublin. The posters show data on the anticancer effects of BAL-101553 in combination with eribulin or gemcitabine for the treatment of advanced metastatic breast cancer and pancreatic cancer, respectively. The first poster showed a highly synergistic anticancer effect of the combination of BAL-101553 with eribulin in in vitro cancer models. The combinations are associated with a dose-dependent significant increase of complete regressions, i.e. cures of up to 80 percent in an animal model of triple-negative breast cancer. The second poster shows that the combination of BAL-101553 with gemcitabine led to complete regression in an animal model of pancreatic cancer, compared to tumor size stabilization (stasis) with gemcitabine alone. Upon treatment cessation, tumors in the gemcitabine monotherapy group regrew while 40 percent to 80 percent of the animals in the combination groups remained in complete regression and were confirmed as cures. The company also presented data showing that BAL-101553 significantly increases the survival duration in an animal model of glioblastoma after long-term oral administration. The survival benefit was largest in tumors expressing the EB-1 protein, which has previously been identified as a potential predictive biomarker of tumor response to BAL-101553.

Bioinvent International AB, of Lund, Sweden, reported publication in *Immunity* of data on the cellular and molecular mechanism of action of antibodies to the co-stimulatory immune checkpoint receptor 4-1BB. It demonstrates that anti-4-1BB antibodies with the ability to engage activating or inhibitory Fc gamma receptors can achieve therapeutic effects through depletion of intratumoral regulatory T cells, and/or boosting of CD8-positive T-cell effector function.

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Adcoms

Continued from page 1

of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Those who voted for approval called the drug a step in the right direction, especially since Mallinckrodt, of Staines-Upon-Thames, U.K., said it would withdraw its current oxycodone IR from the U.S. market if MNK-812 is approved.

Twelve of the panelists supported abuse-deterrent labeling for nasal administration of the drug, but only seven said the data were strong enough to warrant such labeling for I.V. administration. MNK-812 has physical/chemical barriers to manipulation and includes aversive agents that are intended to impede tampering via intranasal and intravenous routes. But it is not impervious to abuse.

In voting against the drug's approval, Jon Zibbell, a senior scientist at RTI International, said there are "already drugs on the market for pain patients." Given the current state of abuse-deterrence science, he advised the FDA to focus on opioid prescribing rather than drugs with abuse-deterrent properties.

Inappropriate prescribing was one of the major public health worries the panelists discussed. The concern is that doctors would read "abuse-deterrent" as "abuse-preventive" or "abuse-proof" and think the opioid is safe to prescribe for a host of aches and pains.

Jeanmarie Perrone, a doctor and professor of emergency medicine at the University of Pennsylvania's Perelman School of Medicine, said abuse-deterrent labeling comes with a huge risk of increased inappropriate prescribing of opioids. Doctors only read the headlines, she said. That, coupled with the lack of standards for the use of opioids in various diagnoses, could make the current crisis worse.

While the FDA supports the development of abuse-deterrent opioids, it is concerned about the potential unintended consequences of well-intentioned products, Sharon Hertz, director of the FDA's Division of Anesthesia, Analgesia and Addiction Products, told the committees. She agreed that the agency needs to work to change how opioids are used in managing pain by fully informing prescribers and patients.

That's a challenge when doctors don't read, or understand, drug labels. "It's no surprise that they're not reading the label," Hertz said. "That's an ongoing problem."

Other impacts the group discussed included the potential spread of infectious diseases through sharing of I.V. doses, needles or straws for snorting oxycodone extracted from the product. There's also the possibility that the advent of abuse-deterrent IR opioids would increase the demand for counterfeits that are easier to manipulate and that could be laced with fentanyl or heroin.

While many of the risks were conjectural, the panel's patient representative, James O'Brien, president and CEO of the National Scoliosis Foundation, pointed out the difficulty of gathering data demonstrating the positives of abuse-deterrence properties. It's not as if individuals will step forward and say they decided not to inject an opioid because of the difficulty caused by an abuse deterrent. But even if one life is saved, that's a positive, O'Brien said.

> *"IR oxycodone is out there. It's used, and it's abused.*
>
> Lonnie Zeltzer
> Director, Pediatric Pain and Palliative Care Program,
> David Geffen School of Medicine

Shades of Opana

The discussion was shadowed by last year's withdrawal of Endo Pharmaceuticals Inc.'s reformulated Opana ER (oxymorphone hydrochloride) due to risks associated with the injection abuse of the product. Although the reformulation wasn't enough to get Opana an abuse-deterrent label, it did result in a significant shift in the route of abuse from nasal to injection. The increase in injection abuse was associated with a serious outbreak of HIV and hepatitis C, as well as cases of thrombotic microangiopathy, a serious blood disorder.

"The Opana experience has given us pause. . . . We don't know what the best answer is here," Hertz said.

The panelists had some suggestions. Perrone told the FDA that it's time to actually regulate rather than just going along with the goals of opioid sponsors.

The committees also urged the agency to start enforcing compliance with its opioid postmarket requirements. For instance, Purdue Pharma LP's reformulated version of Oxycontin has been on the market for eight years, and yet the FDA has no data from its required phase IV studies. "That's unacceptable," said Steven Meisel, system director of medication safety at Fairview Health Services/Healtheast Care System in Minneapolis.

Hertz said the agency's expectation was that the data would be submitted when the sponsors started publishing, but it's hard to force submission. "They don't have to comply," she added.

Should MNK-812 be approved with its proposed label, it would be only the second IR opioid to get abuse-deterrent labeling in the U.S. The first one – Roxybond (oxycodone HCl tablets) – has yet to be launched, even though it was approved in April 2017, according to the FDA briefing documents. Developed by Inspirion Delivery Sciences LLC, Roxybond is to be commercialized in the U.S. by Daiichi Sankyo Inc.

In the meantime, "IR oxycodone is out there," said Lonnie Zeltzer, director of the Pediatric Pain and Palliative Care Program at the David Geffen School of Medicine. "It's used, and it's abused." Approving MNK-812 with abuse-deterrent labeling is worth it, even if it offers only a small improvement, she added. ♦

Cadent

Continued from page 1

phase IIa trial to evaluate the safety, tolerability and efficacy of CAD-1883 in approximately 20 adults with ET, according to Michael Curtis, president and CEO.

SK channels are ion channels that regulate the amount of potassium that enters a cell. In preclinical disease models, CAD-1883 showed the ability to regulate neuronal firing, improve motor control and reduce tremor in individuals with ET. The condition is characterized by uncontrollable shaking or tremor in different parts of the body, including the head, arms, hands, neck and chin, and among the most common movement disorders, affecting 10 million people in the U.S. alone, Curtis pointed out. Nevertheless, no improvements in the standard of care have occurred in more than 40 years.

All told, the round "enables us to run potentially three phase II proof-of concepts – two in movement disorder and one in our second program for cognitive impairment in schizophrenia – over the next two years," Curtis told *BioWorld*.

The schizophrenia program is testing NR2B positive allosteric modulators, subunit selective N-methyl-D-aspartate (NMDA) receptor modulators (SNRMs), for the ability to reverse NMDA receptor hypofunction and restore cognitive balance in people with schizophrenia. Proper functioning of NMDA receptors in the brain is critical for learning, memory and neuroplasticity, and its dysfunction is a significant contributor to cognitive impairment in individuals with schizophrenia. In preclinical studies, Cadent's approach showed the ability to restore auditory novelty detection in a model of NMDA receptor hypofunction.

The B round attracted "a lot of interest," Curtis said, not just for the company's clinical stage programs but also for the diversity of its pipeline, offering "relatively near-term value creators if any one of those phase II studies is positive," since all represent indications with high unmet medical need.

The financing also represented a sort of coming out party for Cadent, which has lain low since its formation.

The backstory began in 2010 when Mnemosyne Pharmaceuticals Inc. was formed by a medicinal chemist and two ex-Pfizer Inc. neuroscientists. That company spent its formative years testing SNRM candidates preclinically for their ability to enhance the activity of the NR2B subtype most prominent in schizophrenia. The goal was to mitigate not only the cognitive symptoms associated with schizophrenia – those least likely to respond to existing antipsychotic drugs – but also to show a therapeutic benefit in the positive and negative symptoms associated with the disease, with fewer side effects than existing antipsychotics.

In 2012, the work attracted a $5.4 million in a Series A financing led by Access Bridgegap Ventures that included the Slater fund as an existing investor. (See *BioWorld Today*, Feb. 16, 2012.)

In 2015, Mnemosyne relocated from Providence, R.I., to Cambridge, Mass., recruited neuroscience R&D veteran Timothy Piser as chief scientific officer (CSO) and was renamed Luc Therapeutics Inc. – short for lucidity – to reflect the company's focus on synaptic plasticity-oriented drug development. Piser had two decades of biopharma leadership, notably at Astrazeneca plc and Forum Pharmaceuticals Inc.

> *"At the end of the day, we're still going to have to show that we've improved quality of life.*
>
> Michael Curtis
> President/CEO, Cadent Therapeutics

Meanwhile, in 2013 Atlas had formed Cambridge, Mass.-based Ataxion Inc. based on promising assets once held by now-defunct Neurosearch A/S. In 2011, Denmark-based Neurosearch decided to focus on a Huntington's disease program – one that would later fail in phase III – and offload its earlier-stage CNS-targeted assets into spinouts. Atlas found the unmet need in ataxia, combined with the biology and the resources already invested in the program, sufficiently compelling to seed the newco.

Rather than attacking individual genetic causes of ataxia, Ataxion was seeking to alleviate the symptoms of a broad range of ataxias by targeting neurons in the cerebellum that are degenerating. In 2014, the company raised $17 million in a series A round from Atlas and Biogen Idec Inc. (now Biogen Inc.). (See *BioWorld Today*, March 31, 2014.)

In March 2017, Ataxion merged into Luc, with a combined focus on precision medicine for neurological and psychiatric diseases and three development programs in the pipeline, including an existing partnership between Luc and Novartis AG testing NR2B subtype selective negative allosteric modulators for rapid, ketamine-like relief of treatment-resistant depression without the ketamine-like side effects. That program subsequently moved into phase I development.

'We're leveraging really powerful biology'

Late last year, Luc quietly rebranded as Cadent, which better reflects the company's mission to restore harmony to neuronal "rhythms," effectively re-wiring the brain to treat movement and cognitive disorders, explained Curtis, whose career has taken him from small-molecule and biologics development at Bristol-Myers Squibb Co. through leadership positions at Genzyme Corp., Infinity Pharmaceuticals Inc. and Catabasis Pharmaceuticals Inc.

In addition to Curtis and Piser, who remains CSO, Cadent's management team includes big pharma veteran Bob Dagher – most recently senior medical director for clinical development services in neuroscience at Covance Inc. – as newly hired chief medical officer and Ataxion alum Gregg Keaney as vice president of product development.

See Cadent, page 8

EORTC

Continued from page 1

triple-negative breast cancer with sacituzumab govitecan (IMM-132), which targets trophoblast antigen 2 (Trop-2). Two or three approvals can be expected in the next few years, he said.

If that scenario comes to pass, it will bolster what is still a sparsely populated drawer in the medicine cabinet.

"We've had a lot of agents that have gone into the clinic – not a lot of them have showed antitumor activity," Anthony Tolcher, CEO of San Antonio, Texas-based phase I clinical research center Next Oncology Inc., told the workshop audience.

A narrow therapeutic index has been the main drag on the development of ADCs over the past two decades, Coats said. Finding the sweet spot that offers a good trade-off between activity and toxicity is the challenge. "It's really threading the needle," he said.

The list of recent casualties includes vadastuximab talirine, a CD33-directed ADC, which Bothell, Wash.-based Seattle Genetics Inc. (Seagen) terminated last year after an undisclosed number of patients died, some from infections, during a phase III trial in acute myeloid leukemia. Earlier this year, Medimmune terminated development of MEDI-4276, a highly potent 'biparatopic' antibody that recognizes two different HER2 epitopes, following a phase I trial in patients with HER2-expressing solid tumors.

Abbvie has not given up the ghost on Rova-T (rovalpituzumab tesirine), the delta-like-protein-3-targeting ADC it gained through its $5.8 billion acquisition (plus up to $4 billion in milestones) of Stemcentrx Inc. Its phase II data in small-cell lung cancer were underwhelming, but the agent is now undergoing several phase III trials in the same indication. A phase I/II combination study with the immune checkpoint inhibitors Opdivo (nivolumab, Bristol-Myers Squibb Co.) and Yervoy (ipilimumab, BMS) is also underway. Abbvie is also running a phase Ib combination trial of Rova-T and its in-house PD-1 inhibitor, ABBV-181.

"We think that combinations of ADCs and checkpoint inhibitors could really enhance the response rate," Alex Bankovich, of Abbvie Stemcentrx LLC, told the session audience.

> *"We think that combinations of ADCs and checkpoint inhibitors could really enhance the response rate.*
>
> Alex Bankovich
> Abbvie Stemcentrx LLC

Coats identified 22 such studies in total, 19 of which are in phase I. The sole phase III combination study underway is a trial of Seagen's Adcetris (brentuximab vedotin) and Opdivo in hematological malignancies. Small-molecule drugs could also potentially enhance the response rate and the durability of responses to ADCs, Bankovich added.

The development of ongoing design enhancements to ADC technology is part of the picture as well. Masking technologies designed to shield healthy tissue from ADC activity – by including additional domains or peptides that are only cleaved in the tumor microenvironment by disease-associated proteases – are being developed by Seagen and Cytomx Therapeutics Inc., among other firms. Those hold out the promise of extending the therapeutic window.

Tolcher also called for "ending the tyranny of microtubule inhibitors," by diversifying the toxic payloads that ADCs carry. Medimmune has three clinical trials underway involving the pyrrolobenzodiazepine (PBD) chemistry it gained through its 2013 acquisition of Spirogen. Several other firms have also licensed that technology. But there are still just three broad classes of payloads – microtubule inhibitors, DNA damaging agents (of which PBD is an example) and topoisomerase inhibitors.

The first ADC carrying a targeted payload entered the clinic this year, Tolcher said. He was unable to discuss the program in any detail but added it was an important step forward for the field.

The meeting continues Thursday. ♦

Other news to note

Dragonfly Therapeutics Inc., of Waltham, Mass., said it entered a new agreement with **Celgene Corp.**, of Summit, N.J., to discover, develop and commercialize immunotherapies for patients with solid and hematological cancers. The deal builds on Celgene's existing four-target collaboration with Dragonfly, signed in 2017, and increases the number of TriNKET immunotherapy drug candidates available for in-licensing by Celgene to a total of eight. The additional four-target deal provides Celgene the option to license exclusive worldwide intellectual property rights to products developed using Dragonfly's TriNKET natural killer cell technology platform in return for a $50 million up-front fee, potential future milestones, potential royalty payments and other material considerations.

Grünenthal Group, of Aachen, Germany, said it has acquired the Morristown, N.J.-based pharmaceutical company **Averitas Pharma Inc.**, which will be responsible for commercializing the pain patch Qutenza (8 percent capsaicin) in the U.S. Earlier in the month, Grünenthal acquired the remaining global rights, including the U.S. rights, for the product from Ardsley, N.Y.-based **Acorda Therapeutics Inc.** Qutenza, a local analgesic, is approved in Europe for a broad peripheral neuropathic pain indication in adults. In the U.S., it is only approved for the treatment of postherpetic neuralgia.

Helix Biopharma Corp., of Richmond Hill, Ontario, said it has developed a two-part strategic plan for the clinical program of L-DOS47. First, programs will focus primarily in a combination setting with well-established chemotherapeutics and in combination with novel immunotherapy. In the second part of the plan, it will focus on expanding the utility of L-DOS47 to indications other than lung cancer and has recently announced the start of a new pancreatic cancer program.

Acquist

Continued from page 1

activators back within normal range, it said.

The data were presented at the American Association for the Study of Liver Diseases.

Uric acid triggers increased fat uptake and inflammation in NASH. Lowering it with ACQT-1127, a bifunctional inhibitor of both xanthine oxidase and URAT1, is expected to block upstream lipogenesis and downstream oxidative stress in humans.

For the one-third of people for whom elevated levels of UA appear to be a central mediator of NASH, "we feel that this and the biology work that has been done presents an opportunity for us to target a biomarker-defined population," Acquist's CEO and founder, Ray Warrell, told *BioWorld*. As the company's small team works to complete an investigational new drug application that would support testing the candidate in both NASH and the more common uric acid-driven indication, gout, it is working to raise a $25 million series A financing, Warrell said. To date, Acquist has raised about $2 million through equity agreements with vendors and from Warrell.

Warrell founded Acquist, formerly called Relburn-Metabolomics, in 2013. The company's work derives from his time at Memorial Sloan-Kettering Cancer Center in New York, where he was an associate physician-in-chief running a number of early stage clinical trials. One of those studies was of a cytotoxic drug from the National Cancer Institute. Despite that trial's focus on cancer, a curious finding emerged, showing that "uric acid was just blown away," even at the lowest dose tested, 100 mg/m2/day. It drew mean serum uric acid concentration down to 1 mg/dL and served as an early prototype for the program Warrell and his colleagues have developed at Acquist.

"Because the biology of uric acid is very different in humans relative to almost every different type of animal species, these happy accidents are just the way things go in gout-land," he said, pointing to examples such as the second-line gout drug Zurampic (lesinurad, Ironwood Pharmaceuticals Inc. and Astrazeneca plc), which he said was a metabolite of an HIV drug originally developed at Ardea Biosciences Inc.

There has been a long history of uric acid being implicated as either a bystander, a mediator or initiator of numerous diseases, including gout, chronic kidney disease, cardiovascular disease and metabolic diseases such as NASH. For more than 50 years, when physicians have sought to treat elevated uric acid levels, they've typically done so by focusing on xanthine oxidase inhibition with drugs like allopurinol or Uloric (febuxostat, Takeda Pharmaceuticals America Inc.). However, almost two-thirds of patients in randomized phase III trials do not respond to those drugs, according to Acquist. Adding inhibition of another enzyme, URAT1, only improves the picture somewhat, a key issue behind the FDA's lukewarm reaction to Zurampic. (See *BioWorld Today*, Dec. 24, 2015.)

The FDA-mandated postmarketing study CARES (Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout and Cardiovascular Disease), which read out in March, just added more emphasis to the need for additional UA-lowering therapies. The study's investigators found that, among patients with gout and cardiovascular disease, Uloric was noninferior to allopurinol at preventing adverse cardiovascular events. Furthermore, they determined that Uloric was associated with an increase in all-cause and cardiovascular mortality, leading to calls by some for it to be pulled from the U.S. market.

> *"Because the biology of uric acid is very different in humans relative to almost every different type of animal species, these happy accidents are just the way things go in gout-land.*
>
> Ray Warrell
> Founder and CEO, Acquist Therapeutics

Moving toward an IND

In addition to Warrell, who has led the company since its inception, Acquist is staffed by its lead chemist, John Piwinski, who was most recently site head and group vice president of Merck & Co. Inc.'s Cambridge, Mass., site and a longtime chemist at Schering-Plough before that. They're joined by John Thottathil, who was most recently chief scientific officer of New River Pharmaceuticals Inc.; Edward Spindler, most recently vice president and head of research and development operations at The Medicines Co. Inc.; John Carbine, who was director of financial strategy at The Medicines Co.; and Brad Zerler, who was vice president, nonclinical development at The Medicines Co.

The team expects to have the IND filed within the first six months of 2019, pending a prompt closing of the series A financing, Warrell said. If approved, it would support a phase I program that, following healthy volunteer studies, will include phase Ia/Ib studies in both NASH and gout, with the goal of determining how to best proceed. ♦

Other news to note

Immunomolecular Therapeutics Inc., of Broomfield, Colo., said it has been awarded a grant from the Small Business Innovation Research (SBIR) program to develop the D enantiomer of methyldopa (D-MDOPA) into an oral small-molecule drug for the preservation of residual beta cell function in type 1 diabetes. Its lead candidate, IMT-002, also was granted rare pediatric disease designation from the FDA. The company said it has conducted a series of studies to evaluate the initial toxicity, pharmacology and metabolic properties of D-MDOPA to establish initial safety parameters, inform future dosing strategies, and further differentiate L-MDOPA from D-MDOPA in terms of in vitro metabolism to support development of a clinical program. To advance D-MDOPA to filing an IND in 2019 and further delineate the drug target effect, the SBIR grant will allow the company to evaluate the direct drug target effect for D-MDOPA both in vitro and in vivo.

Cellanyx

Continued from page 1

prognostics, as well as to be potentially useful in identifying and developing optimum drug regimens and monitoring cancer patients for recurrence. The company published the details of its microfluidics platform, as well as some early data in prostate and breast cancer tissue samples, in the October issue of *Nature Biomedical Engineering* (NBE).

Live cell 'video'

"There are advantages and opportunities that being able to culture live cells from biopsies rapidly enables," Cellanyx co-founder and CEO Ashok Chander told *BioWorld*. "It opens up this new pantheon of biomarkers that were previously inaccessible. So, one way to think about it is if you look at a picture of a family gathering versus a video of a family gathering, you would get so much more insight and information from the video than the picture. You see the dynamic nature of people's faces, the movement and who is interacting with who, etc.

"Similarly, in our ability to keep the cells alive, we're able to see dynamic biomarkers. Biology is not just an historical science or a biographical science, if you will," he added. "It's not just who the players are, but it's about how the players are interacting and when they interact. So, that time component is very powerful and has allowed us to achieve very strong predictive values for our measurements."

The Beverly, Mass.-based company is starting first in prostate cancer with a laboratory developed test that it hopes to have on the market by 2020 or 2021. It's also working in breast cancer, which it anticipates will be the arena of a subsequent test.

Cellanyx is in the midst of raising a second institutional round to support a large, prospective study in prostate cancer for one to two years; that comes on the heels of winning prizes from various universities and incubators, including Mass Challenge and Blue Cross Blue Shield incubator, prior to and since its 2013 founding. Thus far, it has raised only $1.3 million from TIE Boston Angels, Treehouse Health and other private investors.

Prognostication

"When we employ a combination of algorithms, we have demonstrated that we're roughly around 98 percent accurate when it comes to predicting if a patient will have a specific adverse pathology – for example, if a patient will have vascularization or extranodal extension in breast or extra prosthetic extension in prostate," said Chander.

"So, these are important adverse pathologies that doctors already currently use to triage and decide on treatment. The ability to predict them allows them to see into the future, rather than seeing it retrospectively," he continued. "Then they can treat the patient with more information, more foresight and in a more personalized way. That capability and the combination of drug development will also engender really powerful, personalized therapeutics."

In the NBE study, about 5,000 primary live biopsy cells were analyzed for each patient across 26 time points to analyze individual cell morphology and motility. Cells were then fixed for immunohistochemical protein quantification. That generated data on more than 300 features from each cell, primarily focused on adhesion and cytoskeletal markers.

The assay includes a microfluidic device, machine-vision analysis and machine learning algorithm. In the NBE paper, it was trained on features and pathology for 70 percent of the cells with the remaining 30 percent used to then predict disease severity.

Predictive scores were for the risk stratification of 59 prostate cancer patients and 47 breast cancer patients. The study was able to accurately predict the adverse pathology features of the cancer at a rate of greater than 80 percent; higher rates of sensitivity and specificity were achieved depending upon the kind of biopsy tissue sampled.

Further validation

"This work provides a key step forward in stratification of risk to guide cancer prognosis and could provide opportunities for personalized therapy selection and for improving the process of lead-compound discovery for patients with prostate and breast cancer, reducing unnecessary surgical interventions," summed up a commentary on the study data published last month in *Science Translational Medicine*.

"However, one limitation of the study is that each cell was treated as an independent entity, and the model was trained and validated on cells from the same patients," cautioned author Elizabeth Nance, of the Department of Chemical Engineering at the University of Washington. "As cells from the same tumor are likely to have overlapping characteristics, data leak between the training and validation datasets could have occurred, which may have inflated the predictive accuracy of the system. Evaluation in tumors from new patients and other tumors and further validation on risk stratification with a larger patient sample size are key next steps."

Cellanyx is on track to do just that. In a forthcoming paper, the company will detail a much larger prostate cancer dataset in about 250 patients. Another paper slated for 2019 publication will look at a larger dataset in breast cancer to establish the ability to determine which patients are most likely to progress, thereby optimizing the treatment for the most at-risk patients and sparing overtreatment for the lower risk ones. Breast and prostate cancers have both gained a reputation in recent years as often involving aggressive treatment for cancer that may not merit it.

Chander noted that each stage of cancer screening, diagnostics, prognostics and treatment optimization has a relatively low accuracy rate of about 60 percent to 70 percent. So, if the accuracy at each of those stages could be improved, that would be a significant advancement.

"When you start adding up these probabilities of getting a diagnosis, it is actually pretty grim," he summed up. "Being able to add even 10 percent or 20 percent of accuracy in these stages could mean catching eight out of 10 patients as opposed to catching four out of 10 patients." ♦

Cadent

Continued from page 4

Atlas partner Peter Barrett chairs the company's board, which also includes David Grayzel from Atlas, Cowen's Tim Anderson, Paul Wotton of Access and Qiming's Mark McDade.

As the CNS space heats up, three factors set Cadent apart, according to Curtis.

"First, we're leveraging really powerful biology, and doing that in a safe way," he said, noting that the company's use of allosteric modulators, while not new as a mechanism, is being applied in a novel manner. NMDA receptors represent strong and well-validated targets, Curtis added.

"If you take a step back, we're using a dimmer-switch approach," he explained. "In the case of movement disorders and cognitive impairment, we want to turn up the current through the ion channels, and we're doing that through positive modulators. In the case of depression, we want to turn it down."

Recognizing that individuals with essential tremor, ataxia and cognitive impairment may be more different than alike, Cadent also is trying new approaches to patient selection. In ataxia, the company is using a genetic approach that identifies the target population through sequencing. On the cognition side, "the novelty that we bring is an endpoint that allows us to select patients by employing an EEG," Curtis said.

That EEG endpoint also is important to evaluate treatment.

"That's why we love the cognition program so much," Curtis said. "We're going to use an EEG endpoint that allows us to select patients, we're going to use that endpoint also to look at drug response, and that endpoint has been shown to correlate with cognitive impairment. We have a quantitative, measurable biomarker."

Cadent is integrating body sensors and related technologies to build quantitative, objective measures of response into its movement disorder programs. In both cases, the company is confident it can detect early elements of response to its candidates even in relatively small phase II studies.

Although, "at the end of the day, we're still going to have to show that we've improved quality of life" for individuals across its CNS development programs, the FDA is on board with the company's strategy, Curtis said. In fact, the company is working with the agency to qualify its biomarkers and, on the cognition side, is in the early stages of assembling a consortium around its EEG biomarker.

With 10 employees, Cadent remains small but expects to ramp up as its internal programs and partnership with Novartis progress. Curtis predicted the company could have 15 employees by year-end and up to 25 by the end of next year.

After that, "we'll see where the clinical data takes us and where we find the best value for the company," he said. ♦

Other news to note

Institute for Clinical and Economic Review, of Boston, released a report on asthma treatments Dupixent (dupilumab, Sanofi SA/Regeneron Pharmaceuticals Inc.), Xolair (omalizumab, Genentech Inc./Novartis AG), Nucala (mepolizumab, Glaxosmithkline plc), Cinqair (reslizumab, Teva Pharmaceutical Industries Ltd.) and Fasenra (benralizumab, Astrazeneca plc), concluding the drugs produce incremental clinical benefits, but would need to have their prices reduced by at least 50 percent to be cost-effective. A public meeting will be held on Nov. 29 to review the report.

Macrogenics Inc., of Rockville, Md., presented preclinical data for its PD-L1 x CD137 bispecific DART molecule at the 30th EORTC-NCI-AACR Symposium in Dublin. The bispecific molecule was able to stimulate CD137 in a PD-L1-dependent fashion. The PD-L1 x CD137 DART molecules produced T-cell activation and cytokine secretion that was greater than what was produced by the combination of separate PD-L1-blocking and CD137 agonistic monoclonal antibodies. In a mouse model, PD-L1 x CD137 bispecific molecules plus tumor-targeted anti-CD3-based DART molecules enhanced activation of peripheral blood mononuclear cells and inhibited tumor growth.

Mymetics Corp., of Epalinges, Switzerland, presented data on its virosome-based vaccine at the annual Mucosal Vaccines, Adjuvants and Delivery meeting in Lausanne, Switzerland. Mymetics' HIV virosome-based candidate vaccine was transformed into a dry powder and sublingual tablets that were stable for one to three months at 25 and 40 degrees Celsius, while the liquid formulation showed structural degradation at those temperatures. In vivo studies showed nasal delivery of spray dried virosomes and oral delivery of the sublingual tablet triggered immune responses in the serum and mucosal immune compartments.

Notogen Inc., of Menlo Park, Calif., reported preclinical data, published in *Scientific Reports*, showing that NTG-101, its single-dose, injectable protein-based candidate for degenerative disc disease, suppresses known biochemical causes of degenerative discs to very low or undetectable levels while suppressing pro-catabolic processes and stimulating regeneration of the disc extracellular matrix. The candidate also preserves disc height and biochemical properties similar to normal. It showed long-lasting therapeutic effects in canine in vivo subjects and in human disc cells obtained from spinal surgery patients.

Novartis AG, of Basel, Switzerland, said that Alcon Inc., its eye care division, has filed an initial form 20-F registration statement in connection with its previously announced plan to spin off as an independent, publicly traded company. An application is being made to list its shares on the SIX Swiss Exchange and the New York Stock Exchange under the ticker symbol ALC. Completion of the planned spinoff is subject to general market conditions, receipt of necessary authorizations, tax rulings and opinions, final endorsement by the board of Novartis and shareholder approval at the annual shareholder meeting in 2019. If approvals are secured and conditions are met, the spinoff is expected to be completed in the first half of next year.

Precision Biosciences Inc., of Durham, N.C., entered a deal with **Maxcyte Inc.**, of Gaithersburg, Md., for a nonexclusive, clinical and commercial license to use Maxcyte's Flow Electroporation technologies to deliver Precision's Arcus genome-editing technology for use in allogeneic T-cell immunotherapies. Maxcyte is eligible for future undisclosed payments, including milestones and technology access licensing fees. The companies have an existing research and clinical license for the delivery of Precision's Arcus technology into T cells.

Redx Pharma plc, of Alderley Park, U.K., nominated a drug candidate, RXC-006, an oral porcupine inhibitor that it plans to develop for idiopathic pulmonary fibrosis. The company expects to present preclinical data on the RXC-006 at the Anti-Fibrotic Drug Development summit in Cambridge, Mass., on Nov. 29. Clinical trials for the drug are expected to start in 2020.

Regen Biopharma Inc., of San Diego, identified three small molecules that inhibit the NR2F6 nuclear receptor, bringing the total number of drugs in the series to five. Regen plans to study the molecules as potential cancer immunotherapies.

Rxi Pharmaceuticals Corp., of Marlborough, Mass., plans to change its name to Phio Pharmaceuticals Corp. and change its ticker symbol from RXII to PHIO, which will become effective in the coming week.

SVB Financial Group, of Santa Clara, Calif., the parent company of Silicon Valley Bank, said it agreed to acquire Leerink Holdings LLC, the Boston-based parent company of Leerink Partners LLC. The new entity will operate as a wholly owned subsidiary of SVB Financial Group. SVB will acquire Leerink for $280 million in cash up front to the unitholders and, in addition, will provide a retention pool for employees of $60 million to be paid over five years. The deal is set to close in the first quarter of 2019.

United Neuroscience Ltd., of Dublin, presented preclinical data for its Parkinson's disease vaccine, UB-312, at the Parkinson's UK Research Conference held in York, U.K. In in vitro and in vivo mouse studies, as well as in postmortem brain tissue from patients with Parkinson's disease, dementia with Lewy bodies and multiple system atrophy, the vaccine selectively targeted and prevented the accumulation of pathogenic forms of alpha-synuclein proteins.

Virion Biotherapeutics Ltd., of London, presented preclinical data on VH-244 at the 6th International Society for Influenza and other Respiratory Virus Diseases – Advances in Respiratory Virus Therapeutics conference in Washington. In mice, a single dose of VH-244 administered one day before or one, two or three days after injection with pneumonia virus of mice prevented disease and significant weight loss. Repeated dosing didn't lead to resistance.

Appointments and advancements

Alizé Pharma 3, of Lyon, France, appointed Michael Culler chief scientific officer.
Allergy Therapeutics plc, of Worthing, U.K., appointed Scott Leinenweber to its board.
Anavex Life Sciences Corp., of New York, appointed Dag Aarsland to its scientific advisory board.
Anchiano Therapeutics Ltd., of Cambridge, Mass., appointed Stephen Hoffman chair and Robert Connelly to its board.
Azargen Biotechnologies, of Stellenbosch, South Africa, appointed Samuel Fourie to its clinical advisory board.
Azeria Therapeutics Ltd., of Cambridge, U.K., appointed Julian Blagg vice president drug discovery.
Caladrius Biosciences Inc., of Basking Ridge, N.J., appointed Cynthia Schwalm to its board.
Contrafect Corp., of Yonkers, N.Y., appointed Michael Messinger chief financial officer.
Cure Pharmaceutical Corp., of Oxnard, Calif., appointed Alex Katz chief financial officer.
Curevac AG, of Tübingen, Germany, announced the appointment of Ingmar Hoerr, company co-founder and chairman of the supervisory board, as honorary senator by the University of Tübingen.
Effrx Pharmaceuticals SA, of Freienbach, Switzerland, appointed Lorraine Zakin director, medical affairs, Peter Lichtlen chief medical advisor, Christiane Sievert director, regulatory affairs and Victor Papavasileiou vice president, business development.
Hookipa Pharma Inc., of Vienna, appointed Julie O'Neill to its board.
Hox Therapeutics Ltd., of Guildford, U.K., appointed Karl Keegan CEO.
Iaso Biomed Inc., of Centennial, Colo., appointed Lewis Blumenthal, Ravi Kacker, Fred Mermelstein and Barry R. Zirkin to its scientific advisory board.
Insmed Inc., of Bridgewater, N.J., appointed CEO Will Lewis chair of its board. It also appointed Elizabeth McKee Anderson to its board and elected David Brennan lead independent director.
Integra Lifesciences Holdings Corp., of Plainsboro, N.J., appointed Eric Schwartz corporate vice president, general counsel and secretary.
Kiadis Pharma NV, of Amsterdam, the Netherlands, appointed Dirk De Naeyer head of supply chain, Jonathan Sweeting head of commercial Europe and Marcel Zwaal head of corporate development.
Kura Oncology Inc., of San Diego, appointed Mary Szela to its board.
Matrisys Bioscience Inc., of San Diego, appointed Magda Marquet to its board.
Millendo Therapeutics Inc., of Ann Arbor, Mich., appointed Louis Arcudi III chief financial officer and Michael Yeh vice president of medical affairs.
Neon Therapeutics Inc., of Cambridge, Mass., appointed Robert Bazemore to its board.
Nosopharm SAS, of Lyon, France, appointed Sarah Gould chief development officer.
Novavax Inc., of Gaithersburg, Md., appointed Jody Lichaa senior vice president, quality assurance, Brian Rosen senior vice president, commercial strategy, Kathleen Callahan vice president, regulatory affairs, CMC, Susan Hensley vice president, regulatory operations and Brian Webb vice president, manufacturing.
Orchard Therapeutics Ltd., of London, appointed Robin Kenselaar senior vice president and general manager, EMEA commercial operations and Brad Mathis vice president, U.S. commercial operations.
Rexahn Pharmaceuticals Inc., of Rockville, Md., appointed Douglas J. Swirsky president and CEO and to its board.
Tetra Bio-Pharma Inc., of Orleans, Ontario, appointed Steeve Néron senior vice president, marketing and medical affairs.

Financings

Intelgenx Technologies Corp., of Saint Laurent, Quebec, said that Tilray Inc.'s strategic private placement has closed and the company issued 1.42 million common shares at 70 cents each for gross proceeds of $1 million. The company intends to use the proceeds for cannabis-infused Versafilm product development under its previously announced definitive license, development and supply agreement with Tilray.

Prometic Life Sciences Inc., of Laval, Quebec, said it closed its transaction with Structured Alpha LP, extending maturity dates of its $80 million line of credit and original issue discount notes to September 2024.

Synthorx Inc., of La Jolla, Calif., has filed to raise up to $100 million in an IPO. The company is levering its platform technology to develop cytokine synthorins, including IL-2, IL-10 and IL-15, for the treatment of cancer, and another IL-2 synthorin program for the treatment of autoimmune disorders. The company's lead product candidate, THOR-707, is a variant of IL-2 designed to kill tumor cells by increasing CD8-positive T and natural killer cells without causing vascular leak syndrome observed with approved recombinant IL-2 (aldesleukin). It plans to file an IND for the product in the second quarter of next year and initiate a phase I/II trial in multiple tumor types as a single agent and in combination with an immune checkpoint inhibitor. It has applied to list its shares on Nasdaq under the symbol THOR.

Clinical data for Nov. 14, 2018

Company	Product	Description	Indication	Status
Phase I				
Redhill Biopharma Ltd., of Tel-Aviv, Israel	Yeliva (opaganib)	Sphingosine kinase 2 inhibitor	Multiple myeloma	Results from open-label, dose-escalation phase Ib study in refractory or relapsed MM did not show any dose-limiting toxicities; out of 10 evaluable subjects, 2 had stable disease for more than 4 months and 1 patient achieved a very good partial response
Seattle Genetics Inc., of Bothell, Wash.	SEA-BMCA	Antibody targeting B-cell maturation antigen	Multiple myeloma	Dosed first patient in open-label, multicenter, dose-escalation and expansion trial evaluating safety and tolerability in patients with relapsed or refractory MM
Zymeworks Inc., of Vancouver, British, Columbia	ZW-25	Bispecific antibody	Cancer	Induced antitumor activity and was well-tolerated in heavily pretreated patients with a variety of HER2-expressing cancers; overall disease control rate, which includes patients with partial responses and stable disease, was 82%
Phase II				
Attenua Inc., of San Mateo, Calif.	Bradanicline	Agonist of alpha-7 neuronal nicotinic receptors	Cough	Treated first patient in randomized, double-blind, dose-escalation, crossover study testing efficacy and safety in up to 49 patients with refractory chronic cough; additional trials planned for 2019
Axsome Therapeutics Inc., of New York	AXS-05	Dextromethor-phan and bupropion	Major depressive disorder	Completed enrollment in randomized, double-blind, active-controlled ASCEND (Assessing Clinical Episodes in Depression) study; top-line results expected in early January 2019
Bayer AG, of Leverkusen, Germany	Stivarga (regorafenib)	Dual-acting VEGFR 1 to 3, TIE, KIT, RET, BRAF, CRAF, PDGFR and FGFR inhibitor	Glioblastoma	Global Coalition for Adaptive Research and Bayer said regorafenib will be first drug to enter GBM AGILE (Glioblastoma Adaptive Global Innovative Learning Environment), an adaptive platform trial that will evaluate multiple therapies for patients with newly diagnosed and recurrent GBM
Fervent Pharmaceuticals Inc., of Greenville, N.C.	FP-101	Oral version of approved drug; nonhormonal/ nonherbal/non-antidepressant treatment	Vasomotor symptoms associated with menopause	Completed 2-month phase IIa trial in 112 women
Galmed Pharmaceuticals Ltd., of Tel-Aviv, Israel	Aramchol	SCD1 modulator	Nonalcoholic steatohepatitis	Phase IIb data identified aramchol 600 mg as potentially effective to resolve NASH and improve fibrosis; improved liver enzymes and glycemic control; results favor further testing in phase III trial
Novan Inc., of Morrisville, N.C.	SB-206	Topical antiviral gel	Molluscum contagiosum	Preliminary phase II results showed higher rates of complete clearance of all molluscum lesions at week 12 for the 2 highest doses, SB-206 8% and 12% twice-daily, more than double the rate observed in the vehicle group; clear treatment effect observed as early as week 4 in the percent reduction of molluscum lesions; company plans to initiate phase III program in the first half of 2019 with top-line results possible by the end of 2019 or early 2020
Opthea Ltd., of Melbourne, Australia	OPT-302	Soluble form of VEGFR-3	Wet age-related macular degeneration	Completed recruitment in phase IIb study, with 351 treatment-naïve patients enrolled; primary data are expected in the fourth quarter of 2019

Company	Product	Description	Indication	Status
Recro Pharma Inc., of Malvern, Pa.	I.V. meloxicam	Blocks cyclooxygenase	Pain following open abdominal hysterectomy	Data published in *Anesthesia & Analgesia* showed significant analgesic effect, with all doses producing statistically significant improvements vs. placebo in summed pain intensity difference over the first 24 hours post-dose and time-weighted pain relief scores over the first 24 hours post-dose; associated with significantly reduced need for rescue medication (total rescue opioid consumption was 42%-71% lower for all evaluated doses vs. placebo); 3 doses (15 mg, 30 mg and 60 mg) were associated with significantly lower overall rescue opioid consumption vs. the morphine group
Phase III				
Merck & Co. Inc., of Kenilworth, N.J.	Keytruda (pembrolizum-ab)	Anti-PD-1 antibody	Advanced or metastatic esophageal or esophagogastric junction carcinoma	KEYNOTE-181 trial met primary endpoint of overall survival in patients whose tumors expressed PD-L1 (Combined Positive Score [CPS] ≥10); treatment resulted in statistically significant improvement in OS vs. chemotherapy (paclitaxel, docetaxel or irinotecan) in patients with CPS ≥10, regardless of histology; in patients with squamous cell histology and in entire intention-to-treat (ITT) population, results were directionally favorable, though not statistically significant; key secondary endpoints of progression-free survival and objective response rate were not formally tested, as OS was not reached in the full ITT study population
Mithra Pharmaceuticals SA, of Liege, Belgium	Estelle (estetrol 15 mg/ drospirenone 3 mg)	Combination oral contraceptive	Contraception	Completed study, with top-line data on track to be reported in the first quarter of 2019
Notes For more information about individual companies and/or products, see Cortellis.				

Regulatory actions for Nov. 14, 2018

Company	Product	Description	Indication	Status
Eli Lilly and Co., of Indianapolis	Lasmiditan	Oral, centrally penetrant, selective serotonin 5-HT1F agonist	Acute migraine with or without aura	Submitted NDA to the FDA for use in adults
Immunomolecular Therapeutics LLC, of Broomfield, Colo.	IMT-002	Small-molecule D enantiomer of methyldopa	Preservation of residual beta function in type 1 diabetes	FDA granted rare pediatric disease designation
Intrabio Inc., of Oxford, U.K.	IB-1000 compound series	Small molecules	Niemann-Pick disease type A, B and C	European Commission granted orphan medicinal drug designation
Janssen Pharmaceutical Cos., of Johnson & Johnson, of New Brunswick, N.J.	Imbruvica (ibrutinib)	BTK inhibitor	Chronic lymphocytic leukemia	Submitted type II variation application to EMA seeking to expand use to include combination with obinutuzumab in previously untreated adults with CLL and to add long-term follow-up data from RESONATE and RESONATE-2 studies
Janssen Pharmaceutical Cos., of Johnson & Johnson, of New Brunswick, N.J.	Imbruvica (ibrutinib)	BTK inhibitor	Waldenström macroglobulinemia	Submitted type II variation application to EMA seeking to expand use to include ibrutinib plus rituximab in previously untreated and relapsed/ refractory adults with WM

Company	Product	Description	Indication	Status
Merck & Co. Inc., of Kenilworth, N.J.	V-920 (rVSVdeltaG-Zebov-GP, live attenuated)	Vaccine	Ebola Zaire disease	Started submission of a rolling BLA, pursuant to the FDA's breakthrough therapy designation; application expected to be complete in 2019
Regenxbio Inc., of Rockville, Md.	RGX-181	NAV AAV9 vector delivering TPP1 gene directly to CNS	Late-infantile neuronal ceroid lipofuscinosis type 2 disease	FDA granted orphan drug designation for 1 of the most common forms of Batten disease caused by mutations in the TPP1 gene
Stallergenes Greer plc, of London	Oralair (sweet vernal, orchard, perennial rye, timothy and Kentucky blue grass mixed pollens allergen extract)	Allergy immunotherapy sublingual tablet	Grass pollen-induced allergic rhinitis	FDA approved label extension to treat patients, ages 5 to 9
Ultragenyx Pharmaceuticals Inc., of Novato, Calif.	UX-007	Highly purified, pharmaceutical-grade, synthetic, 7-carbon fatty acid triglyceride	Long-chain fatty acid oxidation disorders	Completed a pre-NDA meeting with the FDA and plans to submit NDA in mid-2019

Notes

For more information about individual companies and/or products, see Cortellis.