BioWorld

The news source of record covering the development of innovative human therapies
Actionable Intelligence • Incisive Analysis

Clarivate Analytics

August 28, 2018
Volume 29, No. 167

Tetraphase to take FDA-approved Xerava to market in fourth quarter to treat cIAI

By Marie Powers, News Editor

Tetraphase Pharmaceuticals Inc. turned the commercial corner with FDA approval of Xerava (eravacycline) to treat complicated intra-abdominal infections, or cIAI.

On a conference call following Monday's market close, CEO Guy Macdonald said the company plans to launch the product in October. Pricing is still under review but is expected to be in the range of $200 to $300 per day.

See Tetraphase, page 3

The BioWorld Biome

No AD, but seizures

New complexities uncovered in inflammation's link to Alzheimer's

By Anette Breindl, Senior Science Editor

In findings that underscore the complex roles of inflammation in the brain, researchers have reported that in a transgenic mouse model of Alzheimer's disease (AD), proinflammatory cytokines protected the animals from developing seizures that were severe enough to kill the animals.

They published their results in the Aug. 20, 2018, online issue of the *Proceedings of the National Academy of Sciences*.

Neuroinflammation clearly contributes to the progression of neurodegenerative disease including AD. "Some of us, when we are in a good mood, think that neuroinflammation is everything and that if we could block the inflammation, we could halt [Alzheimer's] disease progression," co-corresponding author Douglas Golenbock half-joked.

See Alzheimer's, page 4

Pfizer's phase III tafamidis study shows reduced ATTR-CM mortality, hospitalization rates

By Michael Fitzhugh, Staff Writer

New data from a phase III study of Pfizer Inc.'s tafamidis in treating the rare and fatal disorder transthyretin amyloid cardiomyopathy (ATTR-CM) showed a 30 percent reduction in the risk of mortality and 32 percent reduction in the rate of cardiovascular-related hospitalizations vs.

See Pfizer, page 5

Roche gets CNDA nod for Alecensa for ALK-positive NSCLC

By David Ho and Elise Mak, Staff Writers

HONG KONG – Roche Holding AG was granted a rapid approval from the China National Drug Administration (CNDA) for Alecensa (alectinib). The drug was greenlighted as a monotherapy treatment for patients with anaplastic lymphoma kinase (ALK)-positive, advanced non-small-cell lung cancer (NSCLC).

See Roche, page 7

In holiday mode

Biopharma companies lag general markets in August

By Peter Winter, Editor

As we head toward the Labor Day holiday weekend, the market performance of the sector's blue chip companies have so far failed to capitalize on their welcomed surge in valuation in July. As a result they are treading water this month with the

See Markets, page 9

World bracing for season, Sanofi ships new flu shots; confident in strains choice

By Randy Osborne, Staff Writer

The long quest for a universal influenza vaccine may soon bear fruit, David Greenberg, associate vice president and regional medical head in North America for Sanofi Pasteur, told *BioWorld*. "We're moving in the right direction," he said, adding that "it's been tough from a research perspective," though his group – the vaccine division of Paris-based Sanofi SA – has been working internally and with collaborators that include the University of Georgia and others. "Progress is definitely being made toward a vaccine that would provide broader protection. I think it's likely that a

See Sanofi, page 6

Prescient plans basket approach to targeting range of cancers

By Tamra Sami, Staff Writer

PERTH, Australia – After reporting positive data at the American Society of Clinical Oncology (ASCO) meeting for its Akt inhibitor in estrogen receptor (ER)-positive breast cancer, Melbourne-based Prescient Therapeutics Pty Ltd. is poised to carve out a niche for itself across a variety of cancers.

Roche AG and Astrazeneca plc generated some excitement about their Akt inhibitors at the recent ASCO meeting this summer, which is bringing new eyes on Melbourne-based Prescient, CEO Steven Yatomi-Clarke told *BioWorld*.

"We're differentiating ourselves with locally advanced estrogen receptor-positive breast

See Prescient, page 8

Other news to note

Amarin Corp. plc, of Bedminster, N.J., said it supported the recent presentation of a scientific poster at the European Society of Cardiology Congress in Munich, Germany, in which analysis indicated that patients with elevated triglycerides (TG) were at a 37 percent higher rate of requiring a procedure for peripheral arterial revascularization per unit time than patients with normal TG levels. These data were based on a retrospective analysis of de-identified medical records from patient experiences within a leading national information and technology-enabled health services business. Patient data from the database were segmented into groups of people with elevated TG levels (≥150 mg/dl, n=22,795) and a control cohort with normal TG levels (<150 mg/dl, n=22,884). This analysis provides evidence to further support that elevated triglycerides are associated with higher rates of peripheral arterial revascularization.

Biocancell Ltd., of Cambridge, Mass., said it is changing its name to Anchiano Therapeutics and will now trade on the Tel Aviv Stock Exchange under the ticker symbol ANCN (formerly BICL). The company is focused on the discovery and development of therapies to treat cancer. It most advanced product candidate, inodiftagene vixteplasmid (BC-819), is in development as a treatment for non-muscle invasive bladder cancer.

Evotec AG, of Hamburg, Germany, said it entered into a global strategic collaboration agreement with **Centogene AG**, of Rostock, Germany, for joint drug discovery projects focused on developing compounds to treat rare genetic diseases. The pact brings together Evotec's leading induced pluripotent stem cell (iPSC) platform and broad drug discovery capabilities with Centogene's medical and genetic insights. In particular, detailed genotype-phenotype data enables rapid biomarker development using patient primary cells. No financial details on the transaction were disclosed.

Lifemax Laboratories Inc., of Palo Alto, Calif., reported an exclusive worldwide license from Basel, Switzerland-based **Novartis Pharma AG** for the right to develop, manufacture and commercialize BPR-277, a clinical stage asset with positive clinical proof of concept for the treatment of Netherton syndrome, an autosomal recessive monogenic disease caused by mutations in the SPINK5 gene that encodes a serine peptidase inhibitor. Symptoms affect the skin, hair and immune systems. The condition in newborns can lead to failure to thrive and can be life threatening. Novartis will receive an up-front payment, development and regulatory milestones as well as royalty on net sales.

Magnolia Neurosciences Corp., of New York, said subsidiary Korysso Therapeutics Inc. was awarded a $19.95 million grant from the Cancer Prevention and Research Institute of Texas (CPRIT) to fund the development of a targeted therapy for the treatment of neurological conditions caused by chemotherapy. Once the grant contract is consummated, CPRIT will fund the advancement of the company's lead molecule through the completion of phase I and into phase IIa development. The company expects to start a phase I trial in the second half of next year.

Pernix Therapeutics Holdings Inc., of Morristown, N.J., said that in the company's litigation against **Alvogen Malta Operations Ltd.**, of Pine Brook, N.J., the U.S. District Court for the District of Delaware found the asserted claims of U.S. Patent Nos. 9,265,760 and 9,339,499, which relate to methods of treating patients with mild and moderate hepatic impairment with hydrocodone bitartrate, to be infringed, but invalid. The litigation relates to Alvogen's submission of an ANDA to the FDA seeking approval to market a generic version of Pernix's Zohydro ER (hydrocodone bitartrate) with Beadtek (hydrocodone bitartrate). Pernix said it would appeal the invalidity ruling.

BioWorld

BioWorld (ISSN# 1541-0595) is published every business day by Clarivate Analytics.

Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement.

Our newsroom

Lynn Yoffee (News Director), Jennifer Boggs (Managing Editor), Peter Winter (*BioWorld Insight* Editor), Marie Powers (News Editor), Anette Breindl (Senior Science Editor), Mari Serebrov (Regulatory Editor), Amanda Lanier (Managing Editor), Karen Pihl-Carey (Analyst), Ann Marie Griffith (Production Editor)

Staff writers: Michael Fitzhugh, Randy Osborne, Shannon Ellis, John Fox, Nuala Moran, Brian Orelli, Alfred Romann, Tamra Sami, Cormac Sheridan

Practical information

For Sales Inquiries: http://clarivate.com/life-sciences/news/bioworld/. NORTH AMERICA, Tel: +1-855-260-5607. Outside of the U.S. and Canada, Tel. +44-203-684-1797. For Customer Service Inquiries, NORTH AMERICA, Tel: +1-800-336-4474. Outside of the U.S. and Canada, Tel. +44-203-684-1796.

For ad rates & information, please contact Evan Raggi at (646) 630-3041, or email evan.raggi@clarivate.com.

For photocopy rights or reprints, please contact Evan Raggi at (646) 630-3041, or email evan.raggi@clarivate.com.

Send all press releases and related information to newsdesk@bioworld.com.

Business office

John Borgman (Director of Commercial Competitive Intelligence), Donald R. Johnston (Senior Marketing Communication Director, Life Sciences)

Contact us

Jennifer Boggs, (770) 880-3631 | John Borgman, (831) 462 2510 | Anette Breindl, (770) 810-3134 | Michael Fitzhugh, (770) 810-3064 | Donald R. Johnston, (678) 641-0970 | Nuala Moran, 44-7778-868-579 | Randy Osborne, (770) 810-3139 | Marie Powers, (770) 810-3136 | Mari Serebrov, (770) 810-3141 | Cormac Sheridan, 353-87-6864323 | Peter Winter, (770) 810-3142 | Lynn Yoffee, (434) 964-4011

Tetraphase

Continued from page 1

Xerava, which did not face an FDA Antimicrobial Drugs Advisory Committee meeting, was greenlighted a day before its PDUFA date to treat cIAI in individuals 18 and older. Its use is restricted to the treatment or prevention of infections proven or strongly suspected to be caused by susceptible bacteria.

Last month, the EMA's Committee for Medicinal Products for Human Use adopted a positive opinion recommending Xerava for approval in the cIAI indication, setting up potential marketing authorization by November across the EU's member countries.

During the phase III program, the synthetic flourocycline antibiotic achieved high clinical cure rates in patients with cIAI, demonstrating statistical non-inferiority to the widely used comparators ertapenem and meropenem. In the 500-patient IGNITE4 study in cIAI, the primary efficacy analysis under FDA guidance was conducted using a 12.5 percent non-inferiority margin in the micro-intent-to-treat population. Clinical cure rates in the group were 90.8 percent and 91.2 percent for eravacycline (n=195) and meropenem (n=205), respectively (95 percent CI: -6.3 percent, 5.3 percent).

Under the EMA guidance, the primary analysis was conducted using a 12.5 percent non-inferiority margin of the modified intent-to-treat (MITT) as well as clinically evaluable (CE) patient populations. Clinical cure rates in the MITT population were 92.4 percent and 91.6 percent for eravacycline (n=250) and meropenem (n=249), respectively (95 percent CI: -4.1 percent, 5.8 percent). Clinical cure rates in the CE population were 96.9 percent and 96.1 percent for eravacycline (n=225) and meropenem (n=231), respectively (95 percent CI: -2.9 percent, 4.5 percent). Eravacycline met the primary efficacy endpoints for both the FDA and EMA guidelines. Secondary analyses were consistent with, and supportive of, the primary outcome. (See *BioWorld*, July 27, 2017.)

No treatment-related serious adverse events turned up in the trial. Treatment-emergent adverse event rates were similar in both treatment groups, and the most commonly reported drug-related adverse events (AEs) for eravacycline were infusion site reactions, nausea and vomiting, each occurring at a rate of less than 5 percent. The AE profile for eravacycline in IGNITE4 was consistent with that seen in the phase III IGNITE1 trial and in phase II cIAI trials.

Tetraphase, of Watertown, Mass., said the spectrum of pathogens in IGNITE4 was similar to that seen in previously completed trials in the patient population, with the most common gram-negative pathogens in the study including *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas* and *Bacteroides*.

Data in the FDA and EMA filings came from IGNITE4, IGNITE1 – which successfully compared eravacycline to ertapenem – and supportive studies. (See *BioWorld Today*, Dec. 19, 2014.)

These phase III IGNITE2 trial, which compared intravenous (I.V.) eravacycline to ertapenem in complicated urinary tract infection (cUTI), fell short by failing to meet the co-primary efficacy endpoints of responder rate (a combination of clinical cure and microbiological success) in the microbiological intent-to-treat (micro-ITT) population at the end-of-I.V. treatment visit and at the test-of-cure visit, which were evaluated using a 10 percent non-inferiority margin. The drug was well-tolerated, with a safety profile consistent with prior studies. (See *BioWorld*, Sept. 10, 2015, and Feb. 15, 2018.)

Earlier this year, Tetraphase officials insisted the cUTI results would not jeopardize the already filed NDA in cIAI. Following the company's second quarter earnings report, H.C. Wainwright analyst Ed Arce was bullish on prospects for approval.

"In those pivotal studies, Xerava demonstrated compelling cure rates across a broad spectrum of multi-drug resistant (MDR) pathogens," Arce wrote in an update.

"Further, unlike some other newer agents, Xerava is effective against both OXA and NDM-1 classes of CRE infections, as well as the most common class, *Klebsiella pneumoniae carbapenemase*," he added. "We believe that this broad coverage is not only highly differentiated but also strongly supportive of a broad label."

CIAIs represent the second most prevalent infection site in hospital intensive care units (ICUs) and the second leading cause of infection-related mortality in U.S. ICUs, according to the company.

Shares of Tetraphase (NASDAQ:TTPH) finished Monday at $3.41 for a gain of 31 cents, or about 10 percent, before trading was halted shortly before market close in advance of the company's announcement. After hours, shares were up another 1 percent. ♦

Other news to note

Photocure ASA, of Oslo, Norway, said an exclusive distribution agreement for the Nordic area for a patented medical device has been signed with **Combat Medical Ltd.**, of Wheathampstead, U.K. The device is designed for the delivery of hyperthermic intra-vesical chemotherapy for non-muscle invasive bladder cancer and has a strong strategic and synergistic fit with current business, Photocure said. Terms were not disclosed.

Specialised Therapeutics Australia Pty. Ltd., of Melbourne, Australia, marked its 10th anniversary by unveiling a new Australian headquarters. The company said it has emerged as the largest privately owned Australian specialty pharma company in the region, employing close to 50 employees, generating revenues of about $30 million, with an expansive specialty drug portfolio spanning oncology, hematology, ophthalmology, supportive care and neurology. Plans for the next 10 years involve in-licensing earlier-stage drugs, steering them through full clinical development and globally commercializing them.

Strategia Holdings LLC, of Boston, disclosed a strategic partnership with **JS Innopharm Ltd.**, of Shanghai, to facilitate global drug development. Through this partnership, both companies will leverage their knowledge, broad expertise, drug candidates, and networks in the global development of multiple therapeutics, Strategia said. Terms were not disclosed.

Alzheimer's

Continued from page 1

Even on less optimistic days, the contribution of neuroinflammation to AD is pretty much undisputed. Previous work by Golenbock and his colleagues has demonstrated that amyloid-beta activates the NRLP inflammasome, a protein complex that sets off inflammatory cell death, and that knocking out inflammasome components protected the animals from developing AD.

Patients with AD, too, have elevated activity of caspase-1, the enzyme that is activated by NRLP3 to set off the processes culminating in cell death.

But the work now published in *PNAS* by Golenbock, co-corresponding author Kensuke Futai, and their colleagues illustrates that there is a potential for anti-inflammatory approaches to AD to have unintended consequences, in the form of detrimental effects on seizure control.

As though AD were not bad enough on its own, one of its consequences is an increased risk of seizures.

"The literature is increasingly clear that most patients with Alzheimer's disease have seizures," Golenbock told *BioWorld*.

Futai pointed out that most of those seizures do not lead to convulsions. Nevertheless, he told *BioWorld*, AD patients have a risk of seizures that, in different studies has been estimated to be elevated from fourfold to a whopping thirtyfold compared to age-matched controls.

Those seizures then further affect memory. At least one case report has shown that an individual with AD who was being monitored had seizures while he was sleeping – at the very time that long-term memories are being formed, Golenbock pointed out – in areas of the brain that are involved in memory consolidation.

"It's clear that it happens, and that it has real effects on patients," Golenbock said.

Based on the earlier work linking the inflammasome, Golenbock and Futai, who are faculty members at the University of Massachusetts Medical School, and their colleagues decided to test the effects of knocking out IL-1beta or IL-18 in transgenic mice expressing familial AD risk genes amyloid precursor protein (APP) and presenilin-1 (PS-1).

Caspase-1, the protein-cleaving enzyme that springs into action when the inflammasome is activated, cleaves both IL-1 and IL-18, and their expectation was that AD mice without those cytokines would be protected from developing AD.

IL-1's effects turned out not to be amenable to study by the approach, since it is necessary for normal brain development, leaving the experiments without a control group.

The team then turned their attention to IL-18, "and after two years realized that we didn't have enough mice to do the experiments," Golenbock recounted. "When IL-18 was knocked out in the AD background, the animals were dying, starting at about two months of age."

Those deaths were a mystery that prompted the team to set up 24-hour video surveillance of the animals. "And that's when we discovered that they were having grand mal seizures and dying," Golenbock said.

For now, the team does not understand in detail why knocking out IL-18 should lead to severe seizures.

"We don't know the mechanism," Futai said. "But when we knock out IL-18… the number of synapses is increased."

That increase, in turn, "somehow boosts the excitatory transmission without affecting inhibitory transmission."

The researchers plan to investigate those molecular mechanisms in greater detail. They also plan to take another look at the role of IL-1beta in both epilepsy and AD with other experimental approaches.

IL-1beta is "the most pro-inflammatory molecule known," Golenbock said, and so there is something of a default assumption that it plays a role in any effect that is mediated by the NRLP inflammasome.

"A lot of people would say it's IL-1beta, there's no question," Golenbock said. "But there's not formal proof of that." ♦

Other news to note

Xbiotech Inc., of Austin, Texas, disclosed the publication of findings that point toward a white blood cell-derived IL1-alpha as a cause of blood clots that could lead to heart attacks or strokes. The research was headed by Peter Libby, Mallinckrodt Professor of Medicine at Harvard Medical School and clinical cardiologist at Brigham and Women's Hospital. His team discovered that white blood cells, known as neutrophils, can release IL-1 alpha that could possibly lead to life threatening strokes in patients with heart disease, which offers the potential for new treatment approaches involving Xbiotech's anti-IL-1 alpha antibody, bermekimab. Findings were published in *Arteriosclerosis, Thrombosis, and Vascular Biology*.

Financings

Harbour Biomed Therapeutics Ltd., of Shanghai, said it completed a series B financing round of $85 million to accelerate the growth of its innovative therapeutic pipeline, including both clinical and discovery stage programs. GIC Private Ltd., Singapore's sovereign wealth fund, led the financing round, with participation from new investors, including China Life Private Equity Investment Co. and Vertex Ventures, and series A investors Advantech and Legend Capital. The company's development programs include an anti-FcRn-based antibody against multiple autoimmune diseases, including myasthenia gravis and neuromyelitis optica, and a biologic against inflammatory dry-eye disease, among its several potential indications.

Novaremed AG, of Basel, Switzerland, said it raised additional financing of CHF6 million (US$6.12 million) from existing shareholders and several new private investors via a rights offering, with pro-rata rights for existing shareholders. The proceeds will be used to prepare for a global phase IIb study of its lead compound, NRD.E1, a first-in-class, small molecule for patients suffering from diabetic neuropathic pain.

Pfizer

Continued from page 1

placebo. The data, presented at the European Society of Cardiology Congress in Munich and simultaneously published online in *The New England Journal of Medicine*, are likely to lay the groundwork for an upcoming U.S. regulatory filing for the drug. However, rather than lifting Pfizer's shares, the news seemed primarily to buoy shares of its competitors, Alnylam Pharmaceuticals Inc. and Ionis Pharmaceuticals Inc.'s, both of which have won U.S. approvals for the treatment of familial amyloid neuropathy, also known as hereditary TTR-mediated amyloidosis (hATTR), an indication that Pfizer's tafamidis is approved for in Europe, but not the U.S.

Shares of Cambridge, Mass.-based Alnylam (NASDAQ:ALNY) climbed by $15.72, or 16.2 percent, to close at $112.59 on Monday. Shares of Carlsbad, Calif.-based Ionis (NASDAQ:IONS) rose too, climbing $3.90, or 7.8 percent, to close at $53.70. New York-based Pfizer's shares fell $0.82, or 1.9 percent, to close at $41.58.

With a "first-mover advantage, we anticipate [Alnylam's] Onpattro will find insulated use in hATTR, which will start with primary [polyneuropathy] patients, likely include a growing 'mixed' (PN and cardiomyopathy) population," Jefferies analyst Maury Raycroft, wrote. "We are unlikely to see much overlap in target opportunities initially for Onpattro and tafamidis," he added. Onpattro gained FDA approval earlier this month. (See *BioWorld*, Aug. 13, 2018.)

Yale Jen, an analyst at Laidlaw & Co., also saw good news in the readout for Ionis which, together with its subsidiary Akcea Therapeutics Inc., gained EMA approval for its hATTR therapy, Tegsedi (inotersen), in July. "We do not believe today's results should create any negative impact on IONS shares given Tegsedi is focusing on the treatment of hereditary PN with potential ease-of- use benefits by subcutaneous delivery," Jen wrote. The FDA has assigned a PDUFA date of Oct. 6 for the drug's U.S. review.

Still, both Pfizer and analysts expect tafamidis could achieve a blockbuster, potentially hitting $1 billion in sales by 2024 according to one analyst's projections. Successfully realizing the program's potential will turn in large part on increasing diagnosis of TTR-CM, Pfizer's Paul Lévesque, said during a conference call held to discuss the ATTR-ACT trial's results. "Pfizer will continue to remain active in educating cardiologists and collaborate with key stakeholders in organizations to support awareness, training, tools to accelerate and expand diagnosis ahead of the potential launch of tafamidis," he said.

Tafamidis, a TTR stabilizer, is marketed as Vyndaqel in Europe and several other ex-U.S. markets, specifically for the treatment of transthyretin familial amyloid polyneuropathy, but has been twice rebuffed by the FDA — initially with a refusal to file letter and later in a complete response letter seeking more evidence of efficacy in the indication. With further data from its phase III ATTR-ACT trial though, the top-line of which was unveiled in April, the company could be well on its way to providing new therapy for TTR-CM patients, who currently have no FDA-approved treatment. (See *BioWorld*, April 2, 2018.)

TTR cardiomyopathy (TTR-CM) comes in two types, TTR familial amyloid cardiomyopathy (TTR-FAC), which is the hereditary form of the disease, and wild-type TTR cardiomyopathy, a non-hereditary form of the disease.

In normal circumstances, the protein TTR transports thyroxine and retinol in the blood. It's made of four identical subunits. When any one of those subunits is mutated though, the configuration becomes unstable, breaking down and leading to the circulation of individual subunits, which are then deposited in tissue as amyloid. When deposited in nerves, that causes polyneuropathy. When deposited in the heart, it causes cardiomyopathy.

In addition to hereditary mutations, age alone can cause the instability that leads TTR's subunits to become unstable and deposit in the heart. People with both that form of the condition – wild-type TTR cardiomyopathy – and TTR-FAC were included in Pfizer's ATTR-ACT study, which tested an oral daily dose of 20 mg or 80 mg tafamidis meglumine capsules compared to placebo.

Awareness of the disease among cardiologists is low, according to Pfizer, with TTR-CM patients often misdiagnosed as hypertensive heart failure patients.

The ATTR-ACT trial showed that tafamidis significantly reduced combined all-cause mortality and frequency of cardiovascular-related hospitalizations compared to placebo over a 30-month period (p=0.0006) in patients with wild-type or hereditary forms of the disorder.

ATTR-ACT was a double-blind, placebo-controlled, randomized, three-arm study in 441 patients with ATTR-CM. It was designed to evaluate the efficacy, safety, and tolerability of an oral daily dose of 20 mg or 80 mg tafamidis meglumine capsules compared to placebo. The study included both patients with variant (ATTRm), or hereditary, form of the disease, and those with wild-type (ATTRwt) form. The primary analysis of the study, which compared a pooled tafamidis (80 mg and 20 mg) treatment group to placebo, was the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalizations over a 30-month period in patients with transthyretin amyloid cardiomyopathy.

The study showed tafamidis significantly reduced all-cause mortality (29.5 percent vs. 42.9 percent; hazard ratio = 0.70, 95 percent confidence interval [CI] 0.51-0.96, p=0.0259) and cardiovascular-related hospitalizations (0.48 vs 0.70 annualized rate; relative risk ratio=0.68, 95 percent CI 0.56-0.81, p<0.0001), compared to placebo. The results represents a 30 percent reduction in the risk of mortality and 32 percent reduction in the rate of cardiovascular-related hospitalization. The findings also showed a consistent directional mortality benefit of tafamidis across all sub-groups.

Secondary study endpoints also showed tafamidis reduced the decline in the six minute walk test distance (p<0.0001), a measure of functional capacity, and reduced the decline in aspects of quality of life measured by the Kansas City Cardiomyopathy Questionnaire – Overall Score (p<0.0001), compared with placebo at Month 30.1 Tafamidis was also well-tolerated, with an observed safety profile comparable to placebo, the company said.

Pfizer has established an expanded access treatment protocol to make tafamidis available to ATTR-CM patients who may benefit from treatment prior to regulatory approval.

So far, tafamidis has been granted orphan status for ATTR-CM in the EU, U.S., and Japan. In June 2017 and May 2018, respectively, the FDA granted it fast track and breakthrough therapy designations for ATTR-CM. Additionally, in March 2018, the Ministry of Labor Health and Welfare in Japan granted the program a Sakigake designation. ♦

Sanofi

Continued from page 1

candidate vaccine would be going into clinical trials in the next year or two. The testing at least is not a decade away, the way we used to talk about it some years ago."

Sanofi Pasteur at the end of last month shipped the first of its nearly 70 million flu vaccine doses to health care providers for the upcoming season. This year's supply uses egg-based and recombinant technologies, and includes increased production of Flublok quadrivalent vaccine and Fluzone high-dose, as well as continued supply of Fluzone quadrivalent. In July 2017, Sanofi made known its plan to acquire Protein Sciences Inc., of Meriden, Conn., for an up-front payment of $650 million and up to $100 million linked to milestones, thereby bringing aboard Flublok.

"We're not producing any standard Fluzone trivalent vaccine any longer, so everything's been converted from Fluzone to quadrivalent, with the exception of our Fluzone high-dose, which is trivalent," Greenberg said. "Clinical trials have been conducted with the Fluzone quadrivalent high dose, and those data will be submitted later this year to the FDA for review and licensure for a future season." Regarding Flublok, "we're going to be supplying more than 10 times the amount of [the vaccine] this coming season than has ever been done by Protein Sciences," he said.

The world is hoping to avoid a repeat of last year's flu season, when the botched vaccine meant misery for people who'd been conscientious about getting the shot. In March, the FDA held an advisory committee meeting on the matter. After hours of poring over flu distribution maps and timelines, along with the genetic characteristics of the various clades and subclades of the influenza strains currently circulating, the panel voted unanimously to advise the FDA to go with the strains the World Health Organization recommended for vaccines in the Northern Hemisphere. "I certainly had the sense that they felt the modifications that were made to the vaccine strains would be a better match" this time around, Greenberg said, and officials seemed even more confident than they had been the season before last. (See *BioWorld Today*, March 2, 2018.)

Converged Markets predicts the flu vaccine market will grow from $4.9 billion in 2017 to $11.4 billion by 2025, at a compound annual growth rate of 11 percent from 2018 to 2025. Key players include: Sanofi; London-based Glaxosmithkline plc; CSL Ltd., of Melbourne, Australia; North Chicago-based Abbvie Inc.; and Astrazeneca plc, of London. "If you go back to 2004, nearly all of the vaccine companies had dropped out" except for Sanofi, Greenberg noted, but competition has picked up since. "Having redundancy is good. In case one manufacturer has a problem, there are others who can cover." Today, between 140 million and 150 million doses are distributed yearly. "We're producing about 70 million of those doses, so we have the lion's share of vaccines being distributed in the U.S., and globally we have about 200 million doses that are distributed from our plants in the U.S. and France. We have between 40 and 50 percent of the market globally and in the U.S."

Greenberg said the "optimal time [to get the shot] is when the vaccine is available in your physician's office or retail pharmacy," since "one doesn't know when the virus is going to start circulating in your community." In some years, the infection rate "picks up very strongly in October," though people may be in the habit of putting it off until Thanksgiving or so. "There's not really any reason to wait," he said. "Some people want to time it to just before the disease hits the area, but you can't predict that. If you have a good response to the vaccine, it's going to protect you through the season."

Diabetes, CV patients at special risk

Flu vaccines have undergone a long evolution. "Years ago, Protein Sciences understood that the vaccine strains through the normal manufacturing process didn't always match the circulating strains very well, so they pushed forward with their recombinant technology," Greenberg said. "That has proven to be very successful," though Sanofi still must "do the best we can in educating physicians, pharmacies, and health systems" about which vaccine best fits certain age groups. "Even today, although the high-dose vaccine has been available since the 2010-2011 season, it still is underappreciated. The original efficacy trial showed about a 24 percent better protection. Since then, there have been another five or six studies that have showed the same."

High-dose Fluzone vaccine is especially suited to people 65 and older, efficacy studies have shown. Most retail pharmacies carry it, Greenberg said, and two-thirds to 70 percent of seniors given a flu vaccine got that one. "For people 50 and over, that's where the Flublok was proven in a randomized, controlled trial to be better than standard vaccine," and it's advisable for adults generally. Efficacy studies showed that Flublok is 30-43 percent better than a standard vaccine. "We're investing in new studies to continue to show its medical benefits," he said, and Sanofi believes the recombinant vaccine "has a strong future." Knowing the differences between shots is important. "We certainly would like patients to ask for specific vaccines, especially those 65 and over," he said.

"In children, the influenza vaccines generally work very well, actually better than in the senior populations and even some of the adult populations," Greenberg said, but persuading their caretakers isn't easy. "In this last season, the Centers for Disease Control [CDC] reported that about 80 percent of children who died of influenza, whose vaccine history was known, did not receive any influenza vaccine," he said.

Not enough adults are convinced for their own welfare, Greenberg said. "They have that presumption that, 'I hear from the news that the vaccines haven't been working that well anyway, so what's the point?'" He acknowledged that the CDC's tracked rates of effectiveness "sometimes can seem disappointing," but said people with existing conditions need to be especially vigilant during flu season. Studies have shown that flu shots "greatly reduced" complications of other problems such as diabetes and cardiovascular (CV) disease, he noted. "Even though most [people] understand that it's more severe than the common cold, they still think of it as being a virus that is going to affect them in the nose and mouth," with cough, runny nose, and congestion the worst symptoms. "They don't make the connection to their diabetes being worse," or to flu as aggravating CV trouble that the person might not have known about, he said. "All it takes is an infection with influenza to actually cause the heart attack or stroke," he said. ♦

Roche

Continued from page 1

Sandra Horning, chief medical officer and head of global product development for Roche, hailed the approval as both a "new era for ALK-positive lung cancer patients in China" and "a significant regulatory shift, with the approval received under unprecedented timelines."

It is now approved in more than 57 countries around the world as a first-line treatment for ALK-positive advanced NSCLC, including the U.S., Europe and Japan. It was approved by the FDA and the EMA in November and December 2017, respectively.

"The rapid approval was based on a priority review as the benefit provided by Alecensa in ALK-positive NSCLC was deemed to meet a significant unmet medical need. Supporting data for this approval include primary analyses from the pivotal phase III ALEX study, in which Alecensa was superior as an initial [first-line] treatment compared with the previous standard of care crizotinib," Anja von Treskow, a spokesperson for Roche, told *BioWorld*.

She added that pharmacokinetics results in Asian patients from the phase III ALESIA study also proved that Alecensa was superior compared to crizotinib in the first-line setting and supporting data from the phase II trials of Alecensa in patients previously treated with crizotinib backed that up.

von Treskow noted that the approval process for this drug was fairly fast.

"Medicine approvals in China used to take more than five years. The CNDA has implemented a series of reforms since last year, which significantly accelerate the review and approval of new drug applications," said von Treskow.

"Hence, the CNDA reforms can shorten the review timelines for innovative medicines, enabling faster access to innovative medicines for patients in China," she added.

"Roche and, above all, Chinese patients are benefiting from CNDA reforms as the reform enables both broader and faster access to innovative medicines for patients in China," said von Treskow.

The Chinese government has also been adamant about bringing a list of much-needed drugs into the country fast. Alecensa happens to be on that list.

On Aug. 9, the Center for Drug Evaluation (CDE) under the CNDA listed 48 drugs that are marketed overseas but not yet available in China, saying it is speeding up the review and approval process for these drugs that are urgently needed in China.

"Regarding the drugs that are not yet registered or are in clinical trials in China, if the applicants believe there is no racial/ethnic differences, they may file an application for marketing directly by submitting overseas clinical data and supporting evidence that shows no such differences," the CDE reported.

Those drugs were to be granted priority review to speed up their entry into the Chinese market. In June, China said the review timeline for imported drugs approved overseas to treat rare diseases would be set at three months.

John C. Balzano, a special counsel in Covington & Burling LLP's food and drug practice group, told *BioWorld* that China's regulatory reform has been anticipated for some time.

"China has recently accepted overseas clinical data and allowed companies to start clinical trials if no objection is raised within 60 days after an application is filed. China committed to this late last year when the government issued a blueprint to reform drug and device regulation," said Balzano.

The goal is to reduce what has previously been a very long timeline to get a clinical trial approved to proceed in China. Balzano anticipates that this would bring China closer with the way this process works in other countries, such as the U.S. and Europe.

"The reorganization of the CFDA (now CNDA) was part of an overall government reorganization in which China combined a number of regulatory functions previously performed by multiple departments into one larger ministry. This created the State Administration for Market Regulation, with the CNDA as a subordinate bureau," said Balzano of the recent overhauls.

"Thus far, the CNDA has been committed to previously initialed reform work in many respects – even issuing a document saying as much – but it is too early to tell how this change will truly affect the trajectory of drug regulation," he adds.

But with the fast approval that Roche has received with Alecensa, this might signify a turn in the tides for the speed of China's drug approval processes. ♦

Prescient

Continued from page 1

cancer," he said, adding, "in some ways it helps having those big guys breaking the ice for us."

Akt plays a key role in the development of many cancers, including breast and ovarian cancer and leukemia. PTX-200 has a novel mechanism of action that specifically inhibits Akt while being comparatively safer.

Most Akt inhibitors work by mimicking ATP, and off-target effects are likely to result in toxicities. PTX-200 inactivates Akt by binding to the PH domain of Akt and preventing its binding to the plasma membrane where it must be localized to be phosphorylated and activated. By preventing Akt binding to the plasma membrane, PTX-200 inhibits Akt, but without the off-target toxic effects of typical kinase inhibitors.

"The thesis is that the aberrant Akt switch drives resistance," Yatomi-Clarke said. "Not only does it make tumors more aggressive, but it contributes to their resistance to therapy. We're seeing this in ovarian cancer where women are resistant to platinum chemotherapy, and we're seeing that with acute myeloid leukemia (AML) where once people relapse they become resistant, and there is very little available for them."

Prescient's phase Ib breast cancer trial evaluated PTX-200 in combination with paclitaxel in women with HER2-negative breast cancer, including triple-negative breast cancer and ER-positive breast cancer.

The trial saw an overall response rate of 50 percent compared to an expected industry average of roughly 25 percent with paclitaxel alone. In patients with locally advanced disease, two patients had complete responses.

The phase Ib trial dosed 28 patients in total, with 16 patients in the dose-escalation stage. By receptor status, responses were particularly encouraging in women with ER-positive disease with a complete response rate of 50 percent and overall response rate of 75 percent, the CEO said.

In patients with locally advanced disease, which is the focus of the phase II study, there were two complete responses (40 percent) and three partial responses (60 percent).

"It looked like the ER–positive patients were more responsive than the triple-negative patients," he said, noting that ER positive is the most common type of breast cancer but difficult to treat with current chemotherapy regimes alone.

The trial had a setback last year when a late-stage cancer patient experienced liver failure and died, and the trial was put on hold. Yatomi-Clarke said the patient had nonalcoholic steatohepatitis (NASH) and, as a result, the FDA wanted to see more liver screenings during the trials. Ultimately, the FDA lifted the hold, and the company updated the risk mitigation plan to minimize risks around hepatotoxicity.

Competitive space

There are no other Akt inhibitors on the market, so this would be a novel therapy, the CEO said.

Roche is developing Ipatasertib, an Akt inhibitor in triple-negative breast cancer. It presented results from its phase II LOTUS study that showed that adding an Akt inhibitor significantly prolonged progression-free survival (PFS).

Astrazeneca's Akt inhibitor Capivasertib is in phase II trials and is being studied in combination with chemotherapy for metastatic triple-negative breast cancer. AZ reported data that showed the addition of the Akt inhibitor significantly increased PFS and overall survival.

PTX-200 is now in a phase II trial in women with HER2-negative locally advanced breast cancer. Five of the patients in the phase Ib study qualify for assessment of phase II data. If at least three complete responses are observed in the first 11 patients, then the phase II trial will expand to another 15 patients. Two complete responses have already been observed in the first five patients, he said.

PTX-200 is also in a phase Ib/II trial in relapsed and refractory acute myeloid leukemia and in a phase 1b/II trial in ovarian cancer. The FDA granted orphan drug designation for PTX-200 in AML.

A basket case study

Prescient's second novel drug candidate, PTX-100 blocks cancer growth enzyme geranylgeranyl transferase-1 (GGT-1) and inhibits activation of Rho, Rac and Ral circuits in cancer cells.

Targeting Ras directly has proven elusive, and PTX-100 disrupts the Ras pathway downstream by inhibiting post-translational modification of Rho, Rac and Ral.

In a phase I trial in advanced solid tumors (mostly gastrointestinal cancers), PTX-100 was well tolerated and achieved stable disease. Prescient plans to target Ras and RhoA mutant malignancies, such as RhoA mutant lymphomas.

It plans to develop a p27 cancer biomarker as a companion diagnostic to potentially identify those patients who are most likely to respond to PTX-100 therapy.

Prescient is following the same development path that Loxo Oncology took with its basket approach to trials rather than looking at specific indications for specific cancers.

Instead, Loxo targeted a number of cancers with the same mutation and bundled them into a basket study. That approach resulted in an enriched patient population across several diseases, and Loxo saw strong data early on, filing its NDA with the FDA based on phase II data.

"Market observers have seen the same thing with Prescient, and that is the same kind of development plan we have," he said, noting that Prescient is about to initiate a pilot study in gastrointestinal cancer, and then is planning to do a basket study in solid tumors and hematology cancers with PTX-100.

The company is running all its trials in the U.S. where recruitment tends to be faster, and could help attract U.S. investors, he said.

"With PTX-200 we might partner, but with PTX-1 00, we could

See Prescient, page 10

Markets

Continued from page 1

value of the BioWorld Biopharmaceutical Index up a modest 0.5 percent at last Thursday's market close compared to a 1 percent increase in the Dow Jones Industrial Average and a 3 percent jump in value for the Nasdaq Composite index. (See BioWorld Biopharmaceutical index, below.)

The flat performance of biopharmaceutical companies is due in part to the quiet period in the market's calendar as investors enjoy holidays rather than peruse daily stock charts.

Healthy year

On the plus side, the group is showing a healthy 6 percent increase year to date supported by a strong 13 percent performance by Amgen Inc. In a research note on the company Jefferies analyst Tom Tarrant noted that it has been a "solid performer" so far this year. "We maintain our BUY as mgmt commentary suggests confidence in guidance – and esp that Neulasta biosimilar launching won't be significant disruption," he wrote. Tarrant also said that instead of playing defense in the face of biosimilar competition, Amgen "could go on the offensive with bolt-on M&A, or in rare scenario big/major M&A, to diversify out the risk, which we think the market will see as positive and the multiple could expand [stock higher]."

Gilead Sciences Inc.'s shares (NASDAQ:GILD) are down 6 percent so far this month eroding much of the gains it recorded in July following a positive second quarter earnings report. The company's market cap has slipped below $100 billion leaving Amgen as the only member supporting this lofty valuation.

Decliners

Leading the decliners in the group is Alexion Pharmaceuticals Inc. (NASDAQ:ALXN) whose shares have dipped 12 percent this month despite closing out July on a high note reporting that second quarter revenues had increased by 14 percent to about $1 billion vs. the second quarter of 2017.

The New Haven, Conn.-based rare disease company saw a 10 percent rise in sales of its leading product, Soliris (eculizumab).

In addition, it announced last week that the FDA had accepted for review its biologics license application (BLA) for approval of ALXN1210, an investigational long-acting C5 complement inhibitor, for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH). The agency has set a PDUFA date of Feb. 18, 2019, as part of an expedited eight-month review.

In addition to the submission in the U.S. and the EU, Alexion said it is preparing a Japanese submission for ALXN1210 as a treatment for patients with PNH.

New York-based Pfizer Inc. has also enjoyed a successful year, seeing its shares (NYSE:PFE) soar 16.5 percent.

The company recently signed a potential $425 million plus royalties collaboration agreement with mRNA specialist Biontech AG. (See *BioWorld*, Aug. 17, 2018.)

The deal covers the development of an influenza vaccine, extending the use of Biontech's mRNA technology focused on cancer to infectious diseases.

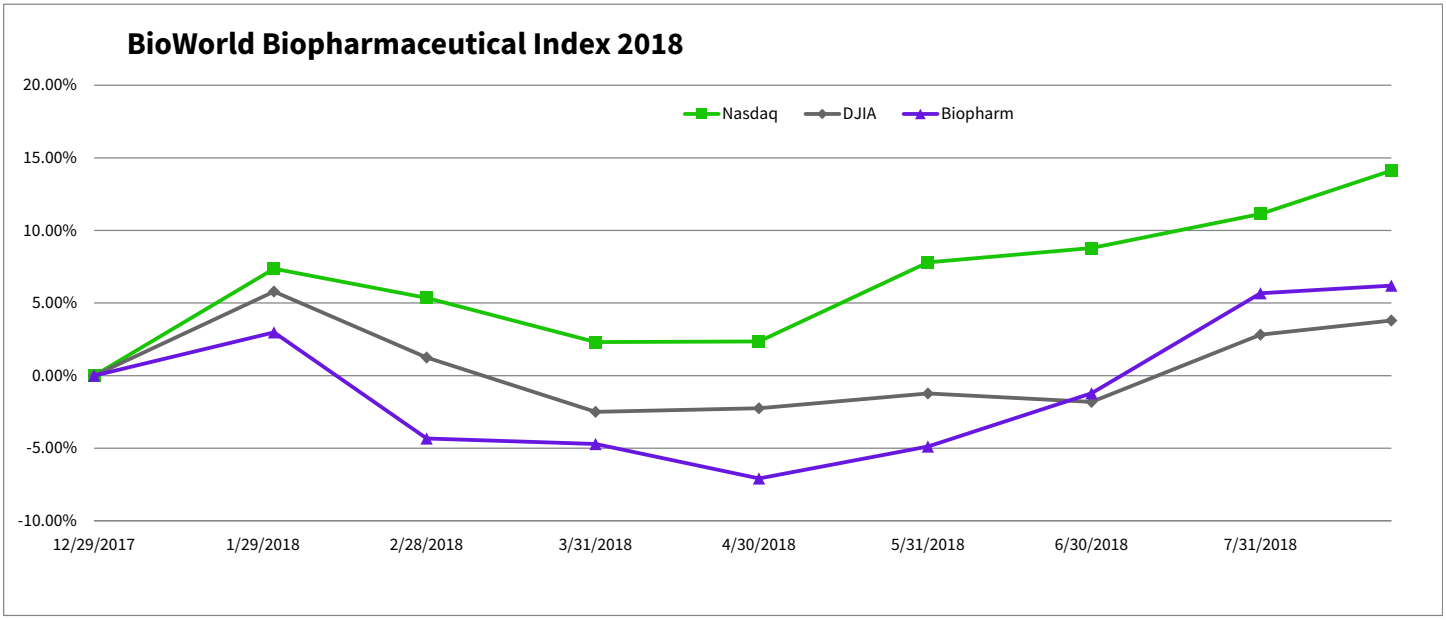
Mainz, Germany-based Biontech will receive $120 million, comprising an up-front payment, an equity investment and research funding to take the vaccine to the end of first-in-human studies. Pfizer will then take on subsequent clinical research and commercialization, with Biontech eligible for up to $305 million in development, regulatory and commercial milestones, plus double-digit royalties on sales if the vaccine makes it to market.

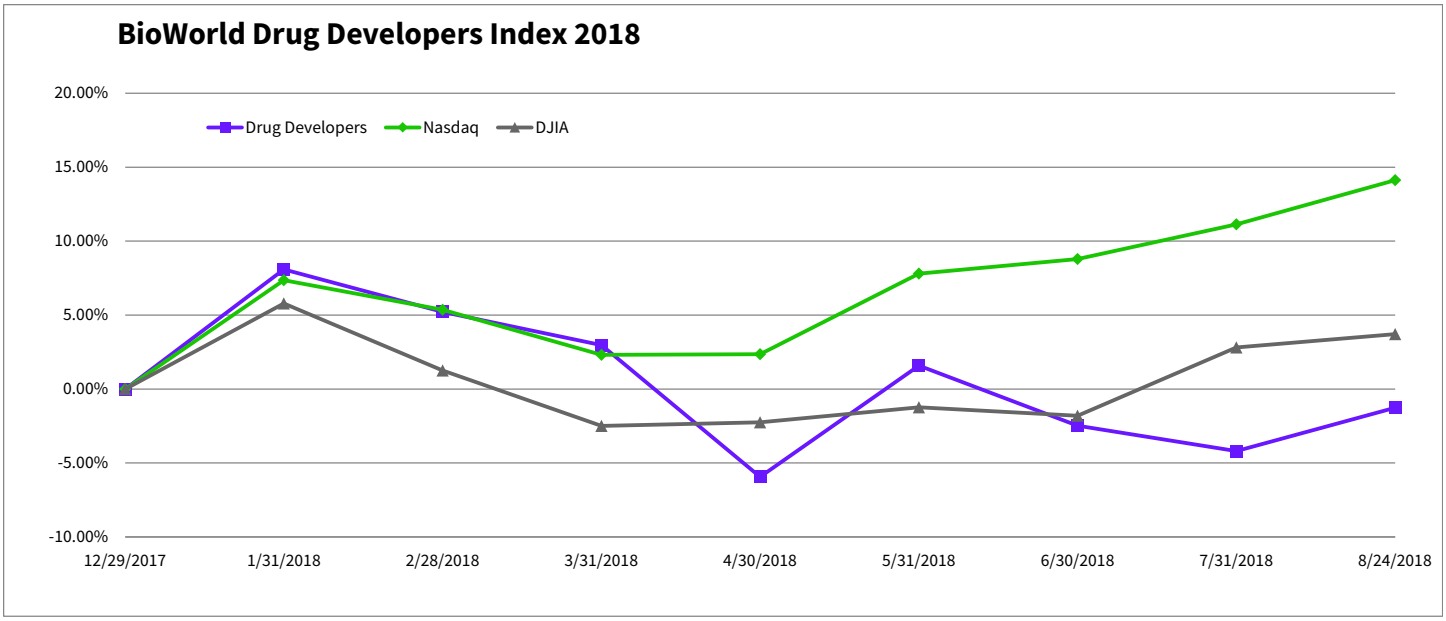
Last week Pfizer also announced that, along with its Japanese partner Astellas Pharma, they have amended protocols for two registrational phase III studies, ARCHES and EMBARK, evaluating prostate cancer drug, Xtandi (enzalutamide) in an expanded patient population to accelerate the anticipated completion timeline for both the studies.

Drug developers

The 3 percent jump in the value of the BioWorld Drug Developers index this month is helping pull the group back to even. Year to date the index is now down only 1.3 percent.

See Markets, page 10





Markets

Continued from page 9

(See BioWorld Drug Developers index, above.)

Leading the gainers in the group is Ardsley, N.Y.-based Acorda Therapeutics Inc. whose shares (NASDAQ:ACOR) are up a healthy 16 percent this month following strong financial results and positive business developments. It beat estimates for sales of Ampyra (dalfampridine), indicated for the improvement of walking ability in multiple sclerosis patients, with 2Q 2018 net sales of $150.3 million compared to $131.6 million for the same quarter in 2017. It reported GAAP net income of $46.2 million for the quarter ended June 30, 2018, or $0.98 per diluted share. GAAP net loss in the same quarter of 2017 was $8.2 million, or $0.18 per diluted share. At June 30, 2018, the company had cash, cash equivalents and short-term investments of $391.7 million.

The company is also waiting on a regulatory decision for Inbrija, an inhaled levodopa candidate for improving motor function in Parkinson's disease (PD) patients. The PDUFA date has been set for Oct. 5, 2018.

Sarepta Therapeutics Inc. also has seen its share (NASDAQ:SRPT) rise 16 percent in August. Earlier this month the Cambridge, Mass.-based company said it made a strategic investment and entered into a license and option agreement with gene therapy company Lacerta Therapeutics Inc. that is deploying adeno-associated virus (AAV) vector technologies to develop CNS-targeted treatments and lysosomal storage diseases. The deal expands Sarepta's footprint in the hot gene therapy field with up to three CNS gene therapy targets.

Surprisingly, the shares (NASDAQ:AGIO) of Agios Pharmaceuticals Inc. have swooned 13 percent in August despite the fact that a full month ahead of its Aug. 21 PDUFA date, its Tibsovo (ivosidenib, formerly AG-120) received FDA approval to treat adults with relapsed or refractory acute myeloid leukemia (r/r AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation. The oral drug became the first FDA-approved therapy in the targeted indication and the first in the class greenlighted with an FDA-approved companion diagnostic, the Abbott Realtime IDH1 test. (See *BioWorld*, July 23, 2018.)

Expectations

Post Labor Day the biopharmaceutical sector could trade sideways for a significant period as the noise levels surrounding the mid-term elections increases. There is no doubt that it will take some blockbuster-type M&A transactions to grab the attention of the generalist investor. It is unlikely that deal flow will slow as companies continue to mine for promising assets to boost their product pipelines. ♦

Prescient

Continued from page 8

realistically carry that ourselves because we have a fast-track development plan," he said.

The company has enough cash to get through this year and deep into next year, he said.

Before coming on board as CEO in February 2016, Yatomi-Clarke was a health care investment banker who was serving on Prescient's board of directors.

Serial entrepreneur Paul Hopper founded the company after coming across the asset from Yale University. The same co-inventor had a second asset that was sitting on the shelf, so Hopper in-licensed both assets and raised funds in Australia in 2014 to set up a company and bring them into the clinic.

With a A$24 million (US$17.5 million) market cap, Prescient's shares on the Australian Securities Exchange (ASX:PTX) are trading at A$0.09. ♦

Regulatory front

Before seeking new regulatory authorities for the 340B program, the U.S. **Health Resources and Services Administration** (HRSA) needs to use the authority it already has, the Democrat and Republican leadership of the **Senate Health, Education, Labor and Pensions Committee** and the **House Energy & Commerce Committee** said in a letter Monday to the agency. Specifically, HRSA needs to issue precise standards for calculating the 340B ceiling prices drug manufacturers can charge eligible providers for the discounted outpatient drugs, set civil penalties for drug companies that overcharge and implement a binding administrative dispute resolution process, according to the letter signed by Sens. Lamar Alexander (R-Tenn.) and Patty Murray (D-Wash.) and Reps. Greg Walden (R-Ore.) and Frank Pallone (D-N.J.). In May, the agency proposed a third delay, until next July, in implementing a rule that would have imposed civil penalties and clarified price calculations for the program.

As part of its implementation of the Drug Quality and Security Act (DQSA), the **FDA** is proposing to keep bumetanide, nicardipine hydrochloride and vasopressin off the list of active pharmaceutical ingredients (APIs) that can be compounded at outsourcing facilities. In explaining the agency's response to requests that the APIs, used in blood pressure and other drugs, be included on the compounding bulk substances list, FDA Commissioner Scott Gottlieb said there's no clinical need for compounding the three substances, as the FDA has approved drugs containing the APIs that can be used or adapted to treat patients with specific needs. Gottlieb described the preliminary decision as a "first-of-its kind action to protect the public health and advance the FDA's implementation of the [DQSA]." Comments on the decision are due in 60 days, according to a notice to be published in Tuesday's *Federal Register*. The agency will take several more steps in the next few months to further implement the DQSA, including issuing a revised draft memorandum of understanding with states to allow a more flexible approach to addressing certain distributions of compounded products. The FDA also plans to issue a revised draft guidance on insanitary conditions at compounding facilities and a revised guidance on current good manufacturing practice requirements that should make it more feasible for 503A pharmacies to become 503B outsourcing facilities, Gottlieb said.

To help it better educate the staff of its Office of Pharmaceutical Quality, the **FDA's Center for Drug Evaluation and Research** is inviting drug companies to submit proposals for its fiscal 2019 site visit training program. Designed to offer experiential and firsthand learning opportunities to provide a better understanding of the challenges that impact a drug's developmental program and commercial life cycle, the site visits involve a tour of participating company facilities, including manufacturing and laboratory operations. The program is open to manufacturers of APIs, drug-device combination products and various forms of finished drugs. Companies interested in participating should submit a proposal by Nov. 22.

The nonprofit **Institute for Clinical and Economic Review** (ICER) issued a report that found the evidence is inadequate to distinguish the clinical benefits of different antiandrogen therapies for men with nonmetastatic castration-resistant prostate cancer. The report assessed the comparative clinical effectiveness of Xtandi (enzalutamide, Astellas Pharma Inc.) and Janssen Biotech Inc.'s Zytiga (abiraterone acetate) and Erleada (apalutamide). Treating men with antiandrogen therapies earlier appears to improve outcomes, said David Rind, ICER's chief medical officer. "Unfortunately," he added, "the lack of long-term survival data and the absence of head-to-head trials limits our ability to compare the effectiveness of enzalutamide with that of the newer drug apalutamide. For abiraterone, we have less certainty in its added benefits when used before cancer progression is detected, making it even more difficult to judge how its effectiveness matches up with the other treatment options." However, the additional costs associated with earlier treatment with all three drugs appear to align with clinical benefits, according to the report, which didn't assess the therapies' value for treating later-stage disease.

As it prepares its annual National Trade Estimate Report on Foreign Trade Barriers, the **U.S. Trade Representative** (USTR) is seeking comments to help it identify significant barriers to U.S. exports of goods and services, U.S. foreign direct investment, and the protection and enforcement of intellectual property rights that should be included in the report. Comments should be submitted by Oct. 30. The USTR also is requesting comments for its annual report to Congress on China's compliance with its World Trade Organization commitments. Those comments, along with requests to testify at an Oct. 3 public hearing on the issue, are due Sept. 19.

Clinical data for Aug. 27, 2018

Company	Product	Description	Indication	Status
Phase I				
Affiris AG, of Vienna	ATH-04, ATH-06	PCSK9 inhibitors	Hypercholest-eremia	72 healthy individuals with slightly elevated LDL-cholesterol (75 to 200 mg/dl) were randomized in 3 parallel treatment groups to ATH-04, ATH-06 or placebo; in second part of study, 50 participants received booster immunization; both immunotherapies were safe and well tolerated
Fit Biotech Ltd., of Tampere, Finland	FIT-06	HIV vaccine	HIV treatment	Delivered first batch of the vaccine to the European HIV Vaccine Alliance for study scheduled to start in the fall; next batch is due in the first quarter of 2019
Forbius (formerly Formation Biologics Inc.), of Austin	AVID-200	Isoform-selective TGF-beta inhibitor	Diffuse cutaneous systemic sclerosis	FDA cleared IND for study evaluating safety, pharmacokinetics, pharmacodynamics and preliminary evidence of efficacy
Morphogenesis Inc., of Tampa, Fla.	ImmuneFx	Autologous cell vaccine	Melanoma	Individuals with unresectable stage III/IV metastatic melanoma will receive the immunotherapeutic vaccine, injected directly as a single agent into the lesion, during a single outpatient visit; some patients will receive the vaccine in up to 3 melanoma lesions
Sienna Biopharma-ceuticals Inc., of Westlake Village, Calif.	SNA-125	JAK3/TrkA inhibitor	Mild to moderate psoriasis	Neither dose reduced patients' inflammatory skin infiltrate thickness from baseline ($p>0.8$); at the lower dose, epidermal thickness was reduced by 17% from baseline ($p<0.05$); plans to start phase II studies in the second half of 2019
Phase II				
Bio-Path Holdings Inc., of Houston	Prexigebersen	Antisense targeting Grb2	Acute myeloid leukemia	First patient dosed in stage 2 of an open-label study testing prexigebersen in conjunction with LDAC; interim analysis expected after approximately 19 evaluable patients
Phase III				
Esperion Therapeutics Inc., of Ann Arbor, Mich.	Bempedoic acid/ezetimibe	ACL inhibitor/ cholesterol absorption inhibitor	Atherosclerotic cardiovascular disease (ACVD) and/or heterozy-gous familial hypercholesterol-emia or multiple risk factors for ASCVD	In study 1002-053, the combination reduced LDL-C by 32% at 12 weeks, compared to 3% for placebo, 21% for ezetimibe alone and 18% for bempedoic acid alone ($p<0.001$ for all 3 comparisons); FDC in high-sensitivity C-reactive protein was reduced by 34% for the combination, compared to an increase of 4% for placebo and reductions of 9% for ezetimibe and 20% for bempedoic acid alone
Janssen Pharmaceutical Co. of New Brunswick, N.J.-based Johnson & Johnson	Xarelto (rivaroxaban)	Factor Xa inhibitor	Acute medically ill patients	In the Mariner study, composite rate of venous thromboembolism (VTE) and VTE-related death was 0.83% for Xarelto and 1.1% for placebo ($p=0.136$); rate of VTE-only events were 0.18% and 0.42%, respectively ($p=0.033$)
Janssen Pharmaceutical Co. of New Brunswick, N.J.-based Johnson & Johnson	Xarelto (rivaroxaban)	Factor Xa inhibitor	Heart failure	In the Commander HF study, composite rate of heart attack, stroke and all-cause death was 25% for Xarelto plus standard of care compared to 26.2% for standard of care alone ($p=0.270$); rate of heart attacks were 3.9% vs. 4.7%, respectively ($p=0.165$) and rate of strokes were 2.0% vs. 3.0%, respectively ($p=0.023$)
Novo Nordisk A/S, of Bagsvaerd, Denmark	Ozempic (semaglutide)	GLP-1 analogue	Type 2 diabetes at high cardiovascular risk	In a post-hoc subgroup analyses of the Sustain 6 trial, reduction in time to first occurrence of non-fatal heart attack, non-fatal stroke or cardiovascular death (MACE) was similar regardless of patients' cardiovascular risk profile at the start of the trial, including whether or not they had a prior heart attack or stroke and whether they had cardiovascular risk factors or established cardiovascular disease; in a post-hoc meta-analysis of the Sustain 1-5 trials, there was a lower risk of MACE in people taking Ozempic, but the result wasn't statistically significant

Company	Product	Description	Indication	Status
Pfizer Inc., of New York	Tafamidis	Stabilizes transthyretin	Transthyretin amyloid cardiomyopathy	In the ATTR-ACT study, tafamidis produced an all-cause mortality rate of 29.5% compared to 42.9% for placebo (HR=0.70, p=0.0259); annualized cardiovascular-related hospitalization rate was 0.48 and 0.70 for tafamidis and placebo, respectively (HR=0.68, p<0.0001)
Phase IV				
Novartis AG, of Basel, Switzerland	Entresto (sacubitril/ valsartan)	Neprilysin inhibitor/ angiotensin receptor blocker	Heart failure patients with reduced ejection fraction	In the Transition study comparing starting Entresto therapy in the hospital or shortly after leaving the hospital, the number of patients who achieved the target dose of 200 mg twice daily at week 10 and the number of patients maintaining 100 mg or 200 mg twice daily for at least two weeks leading to week 10 was similar in both treatment arms
Eisai Inc., of Woodcliff Lake, N.J.	Belviq (lorcaserin HCl)	5-HT 2c receptor agonist	Obesity	CAMELLIA-TIMI 61 cardiovascular (CV) outcomes trial found that long-term treatment with Belviq did not increase incidence of major adverse cardiovascular events (MACE) in overweight and obese patients at high risk for CV event

Notes

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

Regulatory actions for Aug. 27, 2018

Company	Product	Description	Indication	Status
Abbvie Inc., of North Chicago	Imbruvica (ibrutinib) plus Rituxan (rituximab)	Bruton's tyrosine kinase inhibitor + anti-CD20 mAb	Macroglob-ulinemia	FDA approved combination for the treatment of adult patients with Waldenström's macroglobulinemia, based in part on data from the phase III iNNOVATE (PCYC-1127) trial
Beigene Ltd., of Beijing	Zanubrutinib	Bruton's tyrosine kinase inhibitor	Mantle cell lymphoma	China National Drug Administration accepted NDA for the treatment of patients with relapsed/refractory MCL.
Jazz Pharmaceuticals plc, of Dublin	Vyxeos (daunorubicin and cytarabine)	DNA/RNA polymerase inhibitor, liposomal formulation	Newly diagnosed, therapy-related acute myeloid leukemia, AML with myelodysplasia-related changes	Approved by the European Commission
Kite Pharma Inc., of Santa Monica, Calif.	Yescarta (axicabtagene ciloleucel)	Anti-CD19 CAR T therapy	Diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma	European Commission granted marketing authorization for treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma, after two or more lines of systemic therapy
Loxo Oncology Inc., of Stamford, Conn.	Larotrectinib	Tropomyosin receptor kinase inhibitor	Solid tumor	Collaboration partner, Bayer AG, submitted an MAA to the EMA for treatment of locally advanced or metastatic solid tumors with a neurotrophic tyrosine receptor kinase gene fusion
Medical Prognosis Institute A/S , of Hoersholm, Denmark	2X-121	PARP inhibitor	Advanced ovarian cancer	FDA accepted IND for phase II; up to 30 patients will receive 2X-121 600 mg orally daily until progression; primary endpoint is antitumor efficacy (complete remission or partial remission)
Novartis AG, of Basel, Switzerland	Kymriah (tisa-genlecleucel)	Anti-CD19 CAR T therapy	Diffuse large B-cell lymphoma, B-cell acute lymphoblastic leukemia	European Commission granted marketing authorization for the treatment of patients up to 25 years of age with refractory B-cell acute lymphoblastic leukemia in relapse post-transplant or in second or later relapse; and for adults with r/r diffuse large B-cell lymphoma after two or more lines of systemic therapy

Notes

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