



Biogen placates Street, adds Karyopharm neuro asset in potential \$217M deal

By Marie Powers, News Editor

Biogen Inc. reported 2017 revenues of \$12.3 billion, a 7 percent increase compared to full-year 2016 revenues or an increase of 15 percent when revenues from hemophilia assets – ceded last year to spinout Bioverativ Inc. – were excluded. Cambridge, Mass.-based Biogen also reported full-year GAAP net income and diluted earnings per share (EPS) of \$2.5 billion and \$11.92, respectively.

The results generally satisfied analysts, who were even more assuaged by 2018 guidance, which

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Summit shares climb on DMD proof-of-concept data

By Michael Fitzhugh, Staff Writer

Shares of Oxford, U.K.-based Summit Therapeutics plc (NASDAQ:SMMT) rose 12.9 percent to close at \$13.78 Thursday on interim data showing that its Duchenne muscular dystrophy (DMD) candidate, ezutromid, appears to have helped reduce muscle fiber damage and increased levels of a protein called utrophin, seen to offer benefits in restoring and maintaining healthy muscle function. The company said it expects to build on the reported 24-week data with a top-line readout for full 48-week results in the third quarter. Meanwhile, its team will accelerate preparations for the advancement of ezutromid into a pivotal trial, CEO Glyn Edwards said.

The interim data from the open-label trial, called Phaseout DMD, provided the first evidence of target engagement, hinting at proof of concept for Summit's approach to utrophin modulation, which has the potential to be what Edwards called a "universal" therapy for

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Australia's Viralytics adds Chinese investor, raises A\$29M in private placement

By Tamra Sami, Staff Writer

PERTH, Australia – Australia's Viralytics Ltd. is on its way to completing its phase Ib immunotherapy programs of lead candidate Cavatak following a A\$29.6 million (US\$23.9 million) private placement earlier this month with China's Lepu Medical Group.

The placement consisted of about 36.1 million shares priced at A\$2 cents per share, which represented a 27 percent premium, Viralytics CEO Malcolm McColl told *BioWorld*. Lepu will own a 13

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Audentes, Five Prime lead another busy day in public financings

By Jennifer Boggs, Managing Editor

Biopharma's financing frenzy continued Thursday, with eight firms pricing public offerings – six follow-ons and two IPOs – to raise a total of about \$760.7 million before overallotments.

Financings from the first month of the year already had far outstripped money raised in January 2017. (See *BioWorld*, Jan. 24, 2018.)

But this week has been particularly busy, with 15 firms having priced secondary offerings or IPOs, aiming to raise a total of about \$1.39 billion before

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Amoydx receives CFDA approval for lung cancer liquid biopsy test

By David Ho, Staff Writer

HONG KONG – Amoy Diagnostics Co. Ltd. (Amoydx) received CFDA approval for its epidermal growth factor receptor (EGFR) mutation detection kit as a companion diagnostic for EGFR TKI (tyrosine kinase inhibitor)-based non-small-cell lung cancer (NSCLC) drugs.

According to the Xiamen, China-based company, the real-time polymerase chain reaction-based test is designed to identify EGFR mutations in circulating tumor derived fragmented DNA (ctDNA) in plasma samples from patients with advanced or metastatic NSCLC.

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Newco News

Shanghai's EOC Pharma takes a market-led approach to oncology

By Shannon Ellis, Staff Writer

SHANGHAI – EOC Pharmaceutical Group, a specialty pharma with seven cancer assets in its pipeline, has started with the end in mind – not just getting its drugs approved by the CFDA but having them be commercially successful as well.

"We see what is happening in China, and want to move from the commercial side to grow into R&D," said Xiaoming Zou, co-founder and CEO of Shanghai-based EOC, and former chief business officer of Eddingpharm Co. Ltd.

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Financings

Asit Biotech SA, of Brussels, Belgium, said it raised €9.4 million (US\$11.7 million) within the framework of the first phase of the private placement financing approved by the shareholders meeting Dec. 7. A second subscription phase is currently taking place, and the company anticipates subscription of the remaining €2 million of shares that can still be subscribed. Asit is developing immunotherapy products for treating allergies.

Other news to note

Astellas Pharma Inc., of Tokyo, completed the acquisition of **Mitobridge Inc.**, of Cambridge, Mass., and Mitobridge has become a wholly owned subsidiary of Astellas. By exercising the option right to acquire Mitobridge, Astellas paid \$225 million to acquire 100 percent of the firm's equity. Mitobridge shareholders will be eligible for additional payments from Astellas that total up to \$225 million, depending on the progress of various programs in clinical development. The transaction accelerates Astellas' research and development in diseases associated with mitochondrial dysfunctions, the company said. (See *BioWorld*, Dec. 5, 2017.)

Benitec Biopharma Ltd., of Sydney, received a \$4.1 million cash refund for the year ended 2017 under the Australian federal government's R&D Tax Incentive Scheme. The refund relates to the costs of R&D expenditure under the scheme, and the funds will be used to advance Benitec's human therapeutic programs in gene silencing, the company said.

Abcellera Biologics Inc., of Vancouver, British Columbia, disclosed a new therapeutic antibody discovery collaboration with an undisclosed midcap public biopharmaceutical company. The project will take advantage of Abcellera's microfluidic screening platform, including high-throughput single B-cell

selections using cell-based assays, and the ability to perform discovery from alternative species. In addition to research payments, under the agreement Abcellera is eligible to receive milestone payments of up to \$72 million on up to four approved products, as well as low- to mid-single-digit royalty payments on net product sales. Further terms were not disclosed.

Alligator Bioscience AB, of Lund, Sweden, appointed **Theradex Oncology Inc.**, of Princeton, N.J., a global contract research organization, for the planned phase I study of ATOR-1015 for the treatment of metastatic cancer. The study is expected to commence in the second half of 2018. ATOR-1015 is a first-in-class bispecific antibody that targets CTLA-4 and OX40 and was created with Alligator's bispecific technology.

American Gene Technologies International Inc. (AGT), of Rockville, Md., disclosed completion of the pilot runs of its HIV functional cure automated cell processing protocol. That completes a key milestone of the firm's planned phase I trial of AGT103-T, a genetically modified autologous T-cell product in development as an HIV functional cure. The company has produced a GMP-grade lentiviral vector stock that will modify HIV-specific T cells to make them immune to HIV entry and depletion, having fully developed the process for treating cells, in an automated unit, which reliably manufactures the cell product, AGT said.

Anika Therapeutics Inc., of Bedford, Mass., said it established a new agreement with the Institute for Applied Life Sciences at the University of Massachusetts (UMass) to extend their two-year-long strategic collaboration that has so far yielded a promising new modality for the treatment of rheumatoid arthritis (RA). In the next phase of their work, the focus will be on research to optimize the drug delivery system with the goal of advancing a novel therapeutic candidate into clinical trials to support regulatory submission.

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Biogen

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projected revenues of \$12.7 billion to \$13 billion and GAAP and non-GAAP R&D expense of approximately 16 percent to 17 percent of revenue.

Biogen also expanded its neuroscience franchise by acquiring exclusive global rights to develop and commercialize KPT-350, an oral compound from Karyopharm Therapeutics Inc., and other undisclosed assets in exchange for \$10 million up front and up to \$207 million in milestones, plus tiered royalty payments on potential sales. A preclinical selective inhibitor of nuclear export, or SINE, compound, KPT-350 is designed to inhibit exportin 1 (XPO1) with the goal of reducing inflammation and neurotoxicity while increasing neuroprotective responses, aiming to treat amyotrophic lateral sclerosis (ALS) and other neurological and inflammatory conditions.

On Biogen's earnings call, Michael Ehlers, executive vice president and head of R&D, said the company expected to move KPT-350 into a phase I study by year-end.

For Karyopharm, of Newton, Mass., the KPT-350 transaction provides some running room to advance lead asset selinexor (KPT-330), which has advanced into a phase II/III program in multiple myeloma and diffuse large B-cell lymphoma. (See *BioWorld Today*, March 3, 2017.)

"No value is currently in KPTI's stock for KPT-350 or other agents beyond selinexor, representing, in our view, sources of 'free upside,'" Leerink Partners LLC analyst Michael Schmidt wrote in an update on Karyopharm.

"We view this as an incremental positive for KPTI, monetizing an asset that had received virtually no attention or value from the Street, and continue to like KPTI shares into an eventful data year for lead drug selinexor," agreed RBC Capital Markets analyst Brian Abrahams in a first glance at the deal.

H.C. Wainwright's Edward White provided additional color on the structure of the transaction.

"Regarding the other assets, KPT-350 belongs to a patent family that includes other assets and the entire patent family is being transferred to Biogen," he wrote in a first take. "However, Karyopharm believes these assets are of no value."

Karyopharm's focus "remains in executing the development of oral selinexor in oncology," White added. "We believe this transaction bodes well for the company as Biogen, being a leader in the neuroscience franchise, is better suited for the advancement of the drug."

On Thursday, Karyopharm's shares (NASDAQ:KPTI) closed at \$11.80 for a gain of \$1.35, or 13 percent.

For Biogen, the Karyopharm asset, which penetrates the blood-brain barrier to a greater degree than other SINE compounds, supplements existing work in ALS with Ionis Pharmaceuticals Inc.

"This is a key component of nuclear export, and [Karyopharm] had done a lot of collaborative work, very nice scientific work, showing that this could reduce the hallmark pathology of sporadic ALS, which is the cytoplasmic accumulation of

“*An offset, and something to watch, is the sequentially down quarter in new Spinraza patient adds.*”

Christopher Raymond
Analyst, Piper Jaffray

these toxic RNA-binding proteins, like TDP-43 and FUS, which undergo nuclear export that can be blocked in this way," Ehlers explained on the earnings call. Biogen is pursuing the hypothesis that KPT-350 could potentially serve as an oral therapy for sporadic ALS, complementing the BIIIB-067 program, which initially is targeting genetic forms of ALS such as superoxide dismutase (SOD1)-mutant ALS – the second most common form of the familial type of the disease.

"They've got very complementary modalities, completely orthogonal mechanisms and potentially distinct clinical populations," Ehlers said.

'One of the most successful rare disease launches in history'

For the year, Biogen reported that multiple sclerosis (MS) revenues grew 4 percent over 2016, to \$9.1 billion, including \$159 million in royalties from Roche Holding AG on estimated sales of Ocrevus (ocrelizumab), approved last year. For the fourth quarter, MS revenues grew 5 percent, to \$2.3 billion, including \$77 million in estimated Ocrevus royalties, compared to the same period in 2016.

Biogen said U.S. MS revenues in the fourth quarter benefited by approximately \$40 million from increased inventory in the channel, compared to the third quarter, for flagship brands Tecfidera (dimethyl fumarate), Avonex (interferon beta-1a), Plegridy (peginterferon beta-1a) and Tysabri (natalizumab). Full-year global Tecfidera revenues were \$4.2 billion, an increase of 6 percent over 2016, while global Tysabri revenues were stable at \$2 billion.

But the real up-and-comer was Spinraza (nusinersen), developed by long-time partner Ionis. Approved at the end of 2016 to treat spinal muscular atrophy, Spinraza contributed \$884 million in global revenues, including \$657 million in U.S. sales and \$227 million outside the U.S. In the fourth quarter, Spinraza generated \$218 million in U.S. sales and \$144 million in ex-U.S. sales – mainly from Germany, Turkey and Japan. (See *BioWorld Today*, Dec. 28, 2016.)

As of year-end 2017, some 3,200 patients were on therapy across commercial and trial settings, according to Jeffrey Capello, Biogen's new executive vice president and chief financial officer, who called Spinraza "one of the most successful rare disease launches in history."

The sales threshold was achieved despite the fact that, in the fourth quarter and for the year, approximately 20 percent of U.S. Spinraza units were dispensed through Biogen's free drug program, "highlighting our goal that no patient will forgo treatment because of financial limitation or an insurance denial

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Summit

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the full DMD population, addressing all subsets of the disease. So far in Phaseout, treatment with ezutromid appears to have affected a statistically significant and meaningful reduction in muscle damage among participants, as measured by a 23 percent decrease in mean developmental myosin in muscle biopsies vs. baseline. Furthermore, 14 of 22 patients showed a decrease in developmental myosin, with five of those showing a greater than 40 percent reduction, the company said. Mean utrophin protein intensity levels increased by 7 percent in biopsies at 24 weeks compared to baseline.

In a statement accompanying the announcement, Francesco Muntoni, the trial's principal investigator, said the reduction in muscle damage coupled with the increase in utrophin expression seen in the trial participants at 24 weeks "is very encouraging as it suggests ezutromid may slow the relentless cycle of muscle fiber degeneration and regeneration that is a hallmark of DMD."

Functional tests were included as exploratory measures in the study. On the mean six-minute walk distance, participants covered 404 meters at baseline and 395 meters at 24 weeks. On mean North Star Ambulatory Assessment score, a multipoint test of motor function with a maximum score of 34, the baseline score was 25 vs. 24.4 at 24 weeks.

The study also employed magnetic resonance spectroscopy (MRS) to evaluate the amount of fat in muscles, which increases over time in DMD. The mean fat fraction in the thigh was 14.7 percent at baseline and 18.5 percent at 24 weeks (as measured in 37 participants). But longer-term dosing of patients is expected to be required to detect changes in MRS parameters, which is the 48-week primary endpoint.

The clinical significance of the data remains to be determined, Leerink analyst Joseph Schwartz wrote, noting that "novel mechanisms like utrophin modulation might require more data before investors can glean its meaningfulness in DMD."

Other elements remaining to be explored include the impact of age and genotypes on functional clinical outcome, H.C. Wainwright & Co. analyst Debjit Chattopadhyay wrote. "Despite the intriguing data on developmental myosin, we are still some ways away from a systemic oral therapy for DMD; especially the role of ezutromid remains to be teased out over the use of corticosteroids," he added. The brokerage acted as a co-manager in Summit's \$20.1 million public offering of American depositary shares late last year.

For now, the trial will continue. After 48 weeks of treatment, all patients have the option of enrolling into an extension phase, which is gathering long-term MRS, functional and safety data on ezutromid. To date, 18 of 19 eligible patients have enrolled into the extension phase, Summit reported.

In addition to addressing the company's clinical update, Edwards said Summit's cash-on-hand is expected to fund its operations through the end of 2018. During that time, it will plan what is expected to be a randomized, placebo-controlled trial that could potentially support the accelerated

and conditional approval of ezutromid in the U.S. and EU, respectively.

In October 2016, the company negotiated an exclusive license and collaboration agreement with [Sarepta Therapeutics Inc.](#), granting Sarepta an exclusive license to commercialize all of its utrophin modulator pipeline, including ezutromid, in the EU and other territories, with an option to expand its commercial rights to include certain parts of Central and South America. Summit retained commercialization rights to the pipeline in the rest of the world.

In addition to ezutromid, Summit is continuing to work on developing a precision *C. difficile* infection antibiotic called ridinilazole. Efforts to accelerate its progress on infectious disease therapies got a boost in October with its acquisition of U.K.-based Discuva Ltd. for £5 million (US\$7.1 million) in cash and £5 million in new ordinary LSE-listed shares. ♦

In the clinic

Adocia SA, of Lyon, France, reported top-line results from a phase Ib trial evaluating the dose-exposure and dose-response relationships of Biochaperone Combo 75/25 at three different doses in people with type 2 diabetes. Biochaperone Combo combines basal insulin glargine and prandial insulin lispro. Both primary endpoints – the assessments of dose-proportionality for total insulin exposure (AUC_{total}_insulin 0-last) and maximal observed total plasma insulin concentration (C_{max}) across three doses of Biochaperone Combo – were met (AUC₀-last overall dose exposure slope 0.93; 95 percent confidence interval [0.58 ; 1.29] and C_{max} overall dose exposure slope 0.80, 95 percent CI [0.43 ; 1.17]). A dose-proportionality relationship was demonstrated for all exposure pharmacokinetic parameters assessed in the early, intermediate and basal phases.

Other news to note

Astrazeneca plc, of Cambridge, U.K., said the FDA has approved Daliresp (roflumilast) 250 mcg as a starting dose once daily for the first four weeks of treatment followed by 500 mcg thereafter to help reduce the rate of treatment discontinuation in some patients. The drug is currently indicated for reducing the risk of chronic obstructive pulmonary disease (COPD) exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.

Can-Fite Biopharma Ltd., of Petach Tikva, Israel, said it received its first up-front payment of approximately \$2.2 million from **Gebro Holdings GmbH**, of Fieberbrunn, Austria. The company recently entered a distribution agreement with Gebro for the exclusive right to distribute its lead drug candidate, piclidenoson (CF-101), for the treatment of rheumatoid arthritis and psoriasis in three European countries, including Spain, Switzerland and Austria, upon receipt of regulatory approvals. The agreement provides that additional payments of up to approximately \$7 million will be paid upon the achievement of certain regulatory, launch and sales milestones plus double-digit royalty payments on net sales.

Viralytics

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percent stake in Viralytics.

With the funding received from Lepu, as well as another A\$6 million from the federal government in January for the R&D tax credit, Viralytics has about A\$57 million in cash, “which gets us well into 2020 with the full program we’ve got.”

“There are no strings attached to the money,” he said, but “we’re certainly interested in having more discussions with Lepu as we carefully consider our next steps in China.”

Viralytics is developing cancer immunotherapies that harness the power of viruses to infect and kill cancer cells. Lead candidate Cavatak is a genetically unmodified formulation of the common cold virus and is being evaluated in three phase Ib trials in combination with checkpoint inhibitors, including Merck & Co. Inc.’s Keytruda (pembrolizumab) and Bristol-Myers Squibb Co.’s Yervoy (ipilimumab).

McCull is traveling to China next week to learn more about Lepu’s programs as well as to assess the China market to “begin studies in that part of the world.” Clinical programs in lung, colorectal and breast cancers would be good places to start in China, the CEO said.

Beijing-headquartered Lepu Medical Technology is listed on the Shenzhen market and has a market cap around \$6 billion. Until now, Lepu has largely been a medical device company, but it recently decided to enter the pharmaceuticals market.

“They have a PD-1/PD-L1 that is in trials in China,” McCull said. “These guys are well-financed and have a well-developed clinical program, a strong team and ambition to get into the gene therapy field.”

“In China, we’d be able to recruit patients faster and maybe select patients for a sweet spot in lung cancer,” the CEO said.

Preliminary results encouraging

A phase Ib melanoma trial with Cavatak in combination with Keytruda showed an overall response rate of 61 percent and a disease control rate of 78 percent. The preliminary response rates were higher than either therapy used alone. Keytruda alone showed a 33 percent response rate.

A phase Ib combination study with Yervoy and Cavatak in late-stage melanoma, saw a 57 percent overall response rate. Yervoy alone achieved an 11 percent response rate, according to published data. That study is now focused on a subset of melanoma patients who have progressed on prior single-line anti-PD-1 therapy.

McCull said there’s a high unmet need for patients with advanced melanoma who have progressed on checkpoint inhibitors, and Viralytics is planning a phase III pivotal study in 2018. A phase II study that looked at Cavatak as a monotherapy in late-stage melanoma was also completed, which saw an overall progression-free survival rate of 39 percent at six months and one-year survival rate of 75 percent.

The capital raising “will allow us to all complete existing studies, including the Keynote-200 study being conducted in collaboration with Merck,” McCull said.

“

In China, we’d be able to recruit patients faster and maybe select patients for a sweet spot in lung cancer.

Malcolm McCull
CEO, Viralytics

The Keynote-200 study is a two-part study that will compare Cavatak as a monotherapy in patients with late-stage solid tumors, including non-small-cell lung cancer (NSCLC), castrate-resistant prostate cancer, melanoma and bladder cancer. The second stage of the trial will test Cavatak in combination with Keytruda in NSCLC and bladder cancer.

The trial is almost fully enrolled, with 40 patients in lung cancer and 40 patients in bladder cancer. Top-line results are expected in the second quarter, McCull said, noting that the study could readily roll into a pivotal trial.

The Keynote-200 study represents the next big milestone for the company, and it could well be a turning point if the data continue to look as good as they have so far.

“Cavatak has achieved outstanding results in late-stage melanoma patients who have shown long duration of response that are suggestive of an improvement in overall survival. Should these results be repeated in the Keynote-200 trial, the likelihood of a substantial offer for [Viralytics] increases significantly,” wrote Bell Potter analyst John Hester in a December note to clients.

The company plans to expand into head and neck cancer with combination Cavatak and Keytruda; into uveal melanoma with Cavatak and Yervoy; and into colorectal cancer with Cavatak and an undecided checkpoint inhibitor.

The small biotech has the backing of institutional investors that include Orbimed, BVF Partners, Cormorant, Capital Group, Abingworth, Quest and JCP Investment Partners.

With a market cap of A\$173 million, Viralytics lists on the Australian Securities Exchange (ASX:VLA); it also lists under the OTC board as OTCQX:VRACY. The company was up A\$0.73 (1.389 percent) at market close on Thursday. ♦

Other news to note

Eli Lilly and Co., of Indianapolis, said the European Commission has granted marketing authorization for Taltz (ixekizumab), alone or in combination with methotrexate, for the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drug therapies. Ixekizumab selectively binds with interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. This is the second approved indication for ixekizumab in the EU. Ixekizumab was authorized for the treatment of adult patients with moderate to severe plaque psoriasis in adults who are candidates for systemic therapy in Europe in April 2016.

Financings

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overallotments. Leading the pack Thursday was gene therapy firm Audentes Therapeutics Inc., which priced a public offering of 5.75 million shares at \$35 per share for gross proceeds of about \$201.3 million – above the \$150 million initially sought. Another \$30.2 million could be added to the haul if underwriters BofA Merrill Lynch, Cowen, Leerink Partners and Wedbush Pacgrow exercise their full overallotment option of 862,500 shares.

Proceeds from the offering, set to close Jan. 29, will be used to advance several clinical programs, including AT-132, an AAV8 vector containing a functional copy of the MTM1 gene for treating X-linked myotubular myopathy, or XLMTM, a disease that results in extreme muscle weakness, respiratory failure and has an estimated 50 percent mortality by 18 months of age. San Francisco-based Audentes reported positive interim data early this month from the phase I/II ASPIRO study.

Also in the pipeline is AT-342, an AAV8 vector containing a functional version of the UGT1A1 gene, for treating Crigler-Najjar, a disease characterized by extremely high bilirubin levels in the blood and risk of irreversible neurological disease and death. The phase I/II VALENS trial is ongoing. And AT-982, an AAV9 vector carrying the GAA gene to treat Pompe disease, is expected to start phase I/II testing in the fourth quarter of this year.

Audentes, which had \$156 million on its balance sheet as of Sept. 30, said existing cash in addition to the proceeds from the public offering will fund the firm through 2019.

The company went public in July 2016 in a \$75 million IPO, with shares priced at \$15 each. The stock (NASDAQ:BOLD) closed Thursday at \$38.53, up \$3.07. (See *BioWorld Today*, July 21, 2016.)

Up next was cancer immunotherapy-focused Iovance Biotherapeutics Inc., which priced a public offering of about 13 million shares at \$11.50 each, raising gross proceeds of \$150 million. Another \$22.5 million could follow if underwriters purchase the full overallotment. The San Carlos, Calif.-based firm plans to use proceeds for clinical development, including ongoing phase II trials testing LN-144, a tumor-infiltrating lymphocyte (TIL) candidate, in metastatic melanoma and LN-145, a TIL for treating cervical and head and neck cancers.

Jefferies LLC is acting as sole book-running manager for the offering, set to close Jan. 29. Shares of Iovance (NASDAQ:IOVA) closed Thursday at \$14.65, up \$3.15, or 27.4 percent.

Also pricing Thursday was Five Prime Therapeutics Inc., which is selling about 5.1 million shares at \$19.50 per share for gross proceeds of about \$100 million – upsized from an initial plan to raise \$75 million – and net proceeds of about \$93.5 million. Underwriters Goldman Sachs & Co. LLC, J.P. Morgan Securities LLC, Leerink Partners LLC and Wells Fargo Securities LLC have an option to purchase up to 769,230 additional shares, which could bring in another \$15 million in the offering, set to close Jan. 29.

Funds will be used to support pipeline work, including clinical

development of bemarituzumab (FPA-144), an FGF monoclonal antibody for gastric and gastroesophageal junction cancers, and funding Five Prime's portion of the phase I/II FIGHT trial outside of greater China. The company also is advancing cabiralizumab (FPA-008), an IL-34-targeting candidate for pigmented villonodular synovitis and potentially other disorders, and plans to move into the clinic with additional immuno-oncology programs, FPA-150 and FPT-155.

Shares of South San Francisco-based Five Prime (NASDAQ:FPRX) closed Thursday at \$21.51, up \$1.37.

Boston-based Albireo Pharma Inc. priced a \$65 million offering, agreeing to sell 1.97 million shares at \$33 apiece, with underwriters Cowen, William Blair Needham & Co., Wedbush Pacgrow and Roth Capital Partners having a 295,500-share overallotment option that could bring in an additional \$9.8 million in proceeds. The company has been moving forward with plans for phase III testing with A-4250, an ileal bile acid transport inhibitor, in the rare cholestatic liver disease progressive familial intrahepatic cholestasis. Shares of Albireo (NASDAQ:ALBO) closed Thursday at \$34, down \$1.76. (See *BioWorld Today*, April 25, 2017.)

Athenex Inc., of Buffalo, N.Y., is raising \$65.6 million in a follow-on offering of 4.3 million shares priced at \$15.25 per share. Underwriters Deutsche Bank Securities, RBC Capital Markets, Needham & Co., Ladenburg Thalmann and Laidlaw & Co. (UK) Ltd. have an option to purchase up to an additional 645,000 shares, which could add up to \$9.8 million. Earlier this month, the company said it received positive FDA feedback on the ongoing phase III study testing Oraxol, an oral formulation of cancer drug paclitaxel combined with P-gp inhibitor HM-30181A, in metastatic breast cancer. Shares of Athenex (NASDAQ:ATNX) closed Thursday at \$15.10, down 37 cents.

Lastly, Ocular Therapeutix Inc. priced a public offering of 6.5 million shares at \$5 each for gross proceeds of \$32.5 million. Underwriters could add about \$4.9 million if they exercise the overallotment option in full. Bedford, Mass.-based Ocular intends to use the net proceeds, together with its existing cash and cash equivalents, to fund the planned resubmission of its NDA for Dextenza, a corticosteroid intracanalicular insert for the treatment of ocular pain following ophthalmic surgery. The initial submission received a complete response letter last year. Funds also will be used for other candidates and for working capital and general corporate purposes. Piper Jaffray & Co. is acting as sole manager and underwriter. Shares of Ocular (NASDAQ:OCUL) closed Thursday \$5.31, down 88 cents.

Making their debut

Menlo Therapeutics Inc. made a splash Thursday, pricing its IPO of 7 million shares at \$17 per share, the high end of its proposed range. The Redwood City, Calif.-based firm went on to enjoy a warm reception by Wall Street, which sent its newly listed shares (NASDAQ GS:MNLO) up 69 percent on the first day of trading, closing Thursday at \$28.71.

The company is pulling in proceeds of about \$119 million – another \$17.9 million, if underwriters exercise the full

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Amoydx

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“The product is the first adjuvant diagnostic test product approved for methacholic acid mesylate tablets in China, providing a reference for clinicians to formulate individualized treatment plans in clinic,” said the CFDA in a public notice on Monday.

“The CFDA approval means we can start rolling out the diagnostic test in China, which we hope to bring out in that market in about two or three weeks from now,” Harvey Dong, business development manager for Amoydx, told *BioWorld*.

Amoydx said the optimized reaction system of the test kit can offer rapid and accurate mutation coverage that identifies 41 EGFR mutations in exons 18-21, including L858R, exon 19 deletions, and T790M.

“The diagnostic kit promises better sensitivity,” said Dong. It is designed to detect 0.2 percent to 0.8 percent of advanced NSCLC blood ctDNA against a background of 99.8 percent to 99.2 percent normal genomic DNA.

“The test had already received the CE mark for in vitro diagnostic devices in the EU region around April last year,” Dong added. “We will be focusing on commercial labs of hospitals as the target customers for this product.”

There are several EGFR TKIs approved for NSCLC targeted therapy, including first-generation TKIs Iressa (gefitinib, Astrazeneca plc) and Tarceva (erlotinib, Roche Holding AG), second-generation TKI Gilotrif (afatinib, Boehringer Ingelheim GmbH) and third-generation TKI Tagrisso (osimertinib, Astrazeneca plc). Tissue testing has been used for EGFR mutation detection for a long time. However, up to a quarter of patients with advanced or metastatic NSCLC do not have available or sufficient tumor tissue sample for that method of testing.

Without tissue testing as an option, testing for ctDNA in the bloodstream would then be the choice for assessing EGFR mutation status.

Zheng Limou, the founder and CEO of Amoydx, said the CFDA approval for the test kit is significant because it means that patients in China who are unable to provide tissue samples will have an opportunity to receive precision treatment.

The EGFR mutation detection kit is based on Amoydx's super-amplification-refractory mutation system (Super-ARMS) technology.

The liquid biopsy RAS biomarker test tech is easy to use, provides results within 120 minutes, and has been validated on several polymerase chain reaction platforms that are commonly used in diagnostic laboratories, when assessing for KRAS, NRAS and BRAF genes along with other mutations and gene signatures.

In July 2016, Amoydx had teamed up with Merck KGaA to develop a liquid biopsy test for metastatic colorectal cancer for the Chinese market based on the Super-ARMS technology.

“It is now well accepted within the oncology community that understanding the individual RAS biomarker status of metastatic colorectal cancer patients is key to supporting timely treatment decision-making, and results of a recent study

in China further support the efficacy of targeted therapies such as cetuximab in RAS wild-type patients,” said Rehan Verjee, chief marketing and strategy officer of Merck's biopharma business.

The study Verjee referred to was a phase III, open-label, randomized, controlled, multicenter trial designed to compare Merck's Erbitux (cetuximab) in combination with FOLFOX-4 vs. FOLFOX-4 alone in the first-line treatment of patients in China with RAS wild-type colorectal cancer.

Merck and Amoydx plan to implement the Super-ARMS liquid biopsy RAS test for colon cancer in Chinese medical centers first, with a plan to expand into other markets such as Argentina, India, Mexico, Taiwan, Hong Kong, Brazil and Russia by 2019.

Amoydx's portfolio currently covers diagnostics for lung cancer, colon cancer and leukemia. ♦

Other news to note

Hemispherx Biopharma Inc., of Orlando, Fla., said data were presented at the Immuno-Oncology Frontiers conference in Miami detailing the role of combination Ampligen therapy in making the microenvironment of solid tumors more responsive to immuno-oncology agents such as checkpoint inhibitors. The research found that the combinational regimen promotes accumulation of killer T cells in the tumor microenvironment and shows strong therapeutic synergy with checkpoint inhibitors such as anti-PD-1/PD-L1 agents in mouse models of ovarian and colorectal cancers.

Living Cell Technologies Ltd., of Sydney, said it has agreed to sell its 50 percent shareholding in joint venture company Diatranz Otsuka Ltd. (DOL) to the other 50 percent shareholder, Otsuka Pharmaceutical Factory Inc., for \$3 million. Living Cell Technologies (LCT) and DOL have agreed to sign a memorandum of understanding, upon completion of sale of the shareholding, for LCT to exclusively license and use Diabecell, a bioengineered pancreatic islet for the treatment of type 1 diabetes, in Australia, Argentina and New Zealand when it receives FDA approval.

In the clinic

Advaxis Inc., of Princeton, N.J., said data from the investigator-initiated study evaluating the company's Lm-based antigen delivery product, axalimogene filolisbac (ADXS11-001), in combination with chemoradiation as a treatment for high-risk, locally advanced anal cancer were published in the *International Journal of Radiation Oncology*. The phase I study evaluated the safety and preliminary efficacy of the combination of ADXS11-001 with mitomycin, FU and intensity modulated radiation therapy in 10 patients with locally advanced, non-metastatic squamous cell disease. Results showed that nine patients achieved a complete response, and eight patients (89 percent) remained disease-free at a median follow-up of 42 months. One patient progressed, approximately six months post completion of study treatment, and subsequently died from progressive disease, and one patient expired early in the study unrelated to study treatment.

EOC

Continued from page 1

“We believe down the road, when the good times pass, that to have synergy and efficiency is important,” he told *BioWorld*. “That comes with a business model that applies the commercial perspective to R&D.”

Until recently, China’s biotech leaders had to spend a large portion of their days finding creative workarounds to the maze of regulatory delays, like going to Australia for first-in-human studies. But now that the CFDA reforms are underway (since October), China’s preclinical biotechs are waking up to a new challenge: how to ensure they obtain commercial success that will keep their investors happy.

“

In terms of commercial success, it is really a scale game.

Xiaoming Zou
Co-founder and CEO, EOC Pharma

After years of backlogs, China now has roughly 70 to 80 new assets in late-stage development looking to get approved this year or next, according to a McKinsey China report. Its authors pointed out that the “stakes are high for new launches; not everyone will succeed as launch muscles are atrophied.”

The new and urgent need to have robust sales muscle was also an overlooked aspect of the biggest biotech deal of 2017 in China. When Beigene Ltd. sold the global rights to its PD-1 inhibitor to Celgene Corp. for \$1.4 billion, the Chinese firm obtained Celgene’s ready-made commercial operation in China, too.

Fortuitously, 2-year old EOC Pharma – the EOC stands for Eddingpharm Oncology Company – is backed by plenty of commercial experience.

Eddingpharm, EOC’s parent company, was established in 2001 and has a sales force of 1,000 reps behind a portfolio of licensed, brand-established products sold at scale. Yet, Eddingpharm has not been particularly attentive to the cancer space. That is something that its spin-off hopes to rectify with an aggressive push into oncology.

“We believe to move very rapidly into R&D – you can start a lab, but you can also have a two-prong approach: be partnership-driven with a commercial orientation,” said Zou. “We will leverage our experience with KOLs and hospitals, the pipeline we have built and our licensing capability to drive a faster vertical integration in one selective therapeutic area: oncology.”

Building synergy around breast cancer first

EOC’s first area of strategic focus will be breast cancer, with two of its seven assets targeting that indication, with a third marketed breast cancer drug likely to become part of its pipeline as well, should Tykerb (lapatinib) get passed to EOC from Eddingpharm. (Since 2013, Eddingpharm has been selling Glaxosmithkline plc’s HER-targeted therapy in China as a

treatment for advanced metastatic breast cancer.)

Should EOC land Tykerb, it will gain a 40-person team and a salesforce that can reach 380 hospitals, a clinical and commercial advantage that few local biopharmas can boast of.

In December, EOC-202, a first-in-class biologic therapy for breast cancer, received IND approval from the CFDA and “is well on track to enroll patients to the China phase I dose-confirmation trial in [the] first quarter of 2018,” according to Min Dong, senior vice president, clinical development at EOC. EOC-202 (IMP-321), a soluble LAG-3 Ig fusion protein and an APC activator, boosts T-cell responses for metastatic breast cancer.

EOC is co-developing EOC-202 with Prima Biomed Ltd., of Sydney, (which acquired the asset’s originator, Immutep Ltd. SA, of France). Prima is leading a phase II pivotal study in Europe for IMP-321 as a chemo-immunotherapy.

“Recombinant LAG-3 protein is among the hot, next-generation immunotherapy targets and faces limited competition. It has the advantage of its dual mechanism – immune checkpoint inhibitor plus APC activator – which is unique in the LAG-3 space,” said Dong. She added, “EOC-202 has shown impressive activity in conjunction with chemotherapy paclitaxel. It doubles the tumor response rate in a phase I/II metastatic breast cancer trial comparing to historical control, and 90 percent of patients experienced clinical benefit.”

EOC’s second breast cancer candidate is EOC-103 (entinostat), an oral inhibitor of class I histone deacetylases (HDAC) licensed from Syndax Pharmaceuticals Inc., of Waltham, Mass.

The CFDA is expected to greenlight a phase III study for the treatment of women with estrogen receptor-positive breast cancer, the most common form of the disease, and the number one cancer killer for women in China.

Entinostat is already in phase III trials in the U.S. where it received a breakthrough therapy designation from the FDA in 2013 and has shown promising results. (See *BioWorld Today*, May 18, 2017.)

Peeking further into the pipeline, EOC has global rights for two assets acquired from Act Biotech Inc., of San Francisco: EOC-315, a VEGFR inhibitor for gastric cancer preparing for a phase II/III trial in the U.S. and China as well as a phase I bridging study in China; and EOC-317, an FGFR drug for solid tumors, with clinical trial approvals in the U.S. and China.

For its other four assets, EOC retains the rights to China and in some cases other Asian markets.

It also has a second biologic asset under development: EOC-406, a RANKL candidate for bone metastasis licensed from Ablynx NV, of Ghent, Belgium. For China, EOC is in the process of tech transfer, although the candidate has completed a phase I trial in Europe. (See *BioWorld Today*, Oct. 21, 2013.)

Late-stage funding

In November, EOC raised \$32 million from venture investors led by Taikang Investment through Shandong State-owned Taikang Industry Development Fund. H&Q Asia also joined the

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EOC

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round along with series A investor and Eddingpharm backer Sequoia. The funds have been earmarked to further develop the company's pipeline and staffing needs.

"By 2018, we expect to have three programs in late-stage studies in China; that is why we raised more capital," said Zou.

The company got its start with \$10 million in angel investment from Eddingpharm. Shortly after, Sequoia, Bioventure and Eddingpharm kicked in \$15 million for a series A round.

Coming Monday in *BioWorld Insight*

Hospitals seek not-for-profit fix for troubled generic drugs

Talk with the administrators of any given U.S. hospital system, and you'll hear their frustration over shortages of essential medications developed in the 1950s, '60s and '70s – long off-patent – plaguing the U.S. health care system. "You know the market's broken when you have disruptions in supply and you also have wild swings in prices – in many cases, even extortionate prices," said Dan Liljenquist, vice president of the Enterprise Initiatives Office at Intermountain Healthcare in Salt Lake City. The dysfunctional few – most of the generics market is humming along as it should, with easily accessible and reasonably priced medicines, Liljenquist maintained – became the driving force behind an effort spearheaded by Intermountain to create a not-for-profit generic drug company seeking to improve access to drugs that were "left behind" the world of conventional generics.

Looking to boost sales, drugs tackle liver cancer

At the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO-GI) in San Francisco this month, multiple companies presented data on their treatments for hepatocellular carcinoma (HCC), the most common type of primary liver cancer in adults. Like Opdivo (nivolumab, Bristol-Myers Squibb Co.) and Stivarga (regorafenib, Bayer Healthcare Pharmaceuticals Inc.), which received expanded approvals for patients with HCC last year, Exelixis Inc., Aveo Oncology Inc. and Merck & Co. Inc. presented promising data at ASCO-GI for their already-approved drugs – Cabometyx (cabozantinib), Fotivda (tivozanib) and Keytruda (pembrolizumab), respectively – in patients with HCC. Meanwhile, Tracoon Pharmaceuticals Inc. presented early stage data for TRC-105, which isn't on the market yet, but would likely be approved for angiosarcoma before HCC if things go as planned.

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The company currently has 80 people with 40 of them at their 8,000 m2 cGMP facility in Taizhou that can manufacture innovative and generic drugs. The firm also is expanding its clinical and regulatory teams. Once products are approved, those numbers are expected to balloon further.

"In terms of commercial success, it is really a scale game. It is an ability to create sales team synergy, a better cost structure, better penetration – and in terms of R&D, a focused partnership beyond the solid understanding of the shared commercial prospect," said Zou.

EOC Pharma also plans to grow aggressively. It is facing stiff competition from other Chinese biotechs focused on licensing oncology candidates for the China market such as Zai Labs Ltd., of Shanghai, and Lee's Pharmaceutical Holdings Ltd., of Hong Kong, and others developing assets for breast cancer candidates such as Jiangsu Hengrui Medicine Co., of Shanghai. ♦

Financings

Continued from page 6

overallotment – to be used to support completion of its ongoing phase II trials of serlopitant, a once-daily oral NK1 receptor antagonist, for pruritis associated with atopic dermatitis and psoriasis and for refractory cough. Data from the atopic dermatitis study are due in the second quarter, while cough and psoriasis results are due late this year or early next year. (See *BioWorld*, Jan. 3, 2018.)

Menlo also plans to advance its phase III study testing serlopitant for pruritus associated with prurigo nodularis.

Jefferies LLC, Piper Jaffray & Co. and Guggenheim Securities LLC are acting as joint book running managers, while JMP Securities is acting as the lead manager.

Also making its debut Thursday was ophthalmology company Eyenovia Inc., a company focused on development of micro-therapeutics for glaucoma and other eye diseases. It priced an IPO of 2.73 million shares at \$10 per share for gross proceeds of \$27.3 million. Underwriters Ladenburg Thalmann & Co. Inc. and Roth Capital Partners could add up to another \$4.1 million if the full 409,500-share overallotment option is exercised.

Shares of New York-based Eyenovia (NASDAQ:EYEN) ended their first day of trading at \$9.92, down 8 cents. ♦

In the clinic

Eli Lilly and Co., of Indianapolis, published results in *The New England Journal of Medicine* from the two failed phase III trials, EXPEDITION 1 and EXPEDITION 2, testing solanezumab in 1,012 and 1,040 patients, respectively, who have mild to moderate Alzheimer's disease. In EXPEDITION 1, the modeled difference in the change from baseline between groups (solanezumab group minus placebo group) was -0.8 points for the ADAS-cog11 score and -0.4 points for the ADCS-ADL score. In EXPEDITION 2, the difference in ADAS-cog14 was -1.7 points and -1.5 points for patients with mild and moderate Alzheimer's disease, respectively. (See *BioWorld Today*, Aug. 27, 2012.)

Biogen

Continued from page 3

in the U.S.," Capello said.

In the U.S., more than 275 sites submitted start forms and 215 of these dosed at least one patient in 2017, Capello said on the earnings call. The number of patients on therapy in the U.S. increased by 33 percent in the fourth quarter compared to the end of the third quarter, although revenues from the fourth quarter grew at a lower rate than patients, which he attributed to loading dose dynamics.

"We're seeing an increase in contribution for maintenance doses as patients who started earlier in the year transitioned to dosing once every four months on a chronic basis," Capello explained. Roughly one-fourth of Spinraza's U.S. revenues in the fourth quarter were attributed to maintenance doses, compared to 10 percent in the third quarter. "We expect this dynamic to normalize over time, with approximately 50 percent of revenue being driven by maintenance doses by the end of 2018," he said.

In 2018, Biogen expects continued revenue growth from Spinraza in the U.S. but "a larger portion of the revenue growth to come from outside U.S.," Capello said, both in existing territories and from expansion into additional countries.

Biogen reported cash, equivalents and marketable securities of approximately \$6.7 billion and approximately \$5.9 billion in notes payable and other financing arrangements as of Dec. 31, 2017.

In all, the Biogen story was sufficiently strong for Cowen and Co. analyst Eric Schmidt to raise the company's price target to \$408 from \$338.

"Biogen reported impressive top-line results, although EPS missed on one-time fluctuations," he wrote in a flash note. "The MS franchise continues to weather the Ocrevus launch well. Spinraza sales were strong as the drug's ex-U.S. launch has accelerated, [and] 2018 guidance also exceeded expectations." Piper Jaffray's Christopher Raymond noted that, "While some may rightly quibble that inventory build was a critical driver of the quarter, we think the broader theme remains that Ocrevus' impact to BIIB's MS franchise has stabilized and may not be as bad as once feared."

Raymond was a bit wary of the fourth-quarter Spinraza story, however.

"An offset, and something to watch, is the sequentially down quarter in new Spinraza patient adds," he wrote in an earnings note. "While management blamed holiday seasonality, the fact that the Spinraza sales force was doubled in Q4 makes us wonder if there is more urgency to find the all-important source of growth – new patients. For now, we maintain our FY18 Spinraza estimate of \$1.7B (consensus \$1.577B), but are mindful of this dynamic."

And of M&A prospects, Jefferies Group LLC's Michael Yee wrote that Biogen "emphasized the \$37B+ of 'capacity,' which, in our view, makes clear their ability to do a 'material' deal if they are needed." He cited Sage Therapeutics Inc. and Avexis Inc. as examples of companies with the synergy "to really move the

needle beyond 2019+, or fix the 'tail risk' the Street sees with Spinraza."

On Thursday, Biogen's shares (NASDAQ:BIIB) gained \$7.24 to close at \$353.74. ♦

Other news to note

Novartis AG, of Basel, Switzerland, said it signed a licensing agreement with **Spark Therapeutics Inc.**, of Philadelphia, covering development, registration and commercialization rights to voretigene neparvovec in markets outside the U.S. Known as Luxturna (voretigene neparvovec-rzyl) in the U.S., the product received FDA approval in December as a one-time gene therapy to restore functional vision in children and adult patients with biallelic mutations of the RPE65 (retinal pigment epithelial 65 kDa protein) gene. A market authorization application with the EMA was filed at the end of July. In an 8-k filing, Spark reported it will receive an up-front payment of \$105 million and be eligible to receive an additional \$25 million in cash if investigational voretigene neparvovec is approved by the EMA as well as up to \$40 million in cash based on receipt of initial sales outside the U.S. in certain markets. The company said it is also entitled to receive royalty payments at a flat mid-twenties percentage of net sales on a royalty-region by royalty-region basis. Spark will retain exclusive rights for the product in the U.S. and will have the responsibility for obtaining EMA approval. Commercialization rights will be transferred to Novartis upon successful completion of registration and issuance of market authorization. Novartis has exclusive rights to pursue development, registration and commercialization in all other countries outside the U.S. (See *BioWorld*, Dec. 20, 2017.)

Novelion Therapeutics Inc., of Vancouver, British Columbia, said it is implementing significant cost reduction plans to manage its cash resources and the effects brought about by the delay and uncertainty of the settlement of its Aegerion Pharmaceuticals subsidiary with the U.S. Department of Justice and the Securities and Exchange Commission. In addition to work force and other cost reductions, the company said it is pursuing licensing opportunities for its zuretinol drug candidate designed to treat certain rare inherited forms of blindness that predominately affect children.

Partner Therapeutics Inc., of Boston, has been launched by executives Robert Mulroy and Debasish Roychowdhury to focus on commercial and late-stage cancer therapies. The company intends to work on the entire range of cancer therapy from primary treatments to supportive care. Roychowdhury will serve as chief medical officer and director of the company and Mulroy will serve as chairman and CEO.

Prokaryotics Inc., of Union, N.J., said it entered a licensing agreement with **Merck & Co. Inc.**, of Kenilworth, N.J., and it will gain worldwide rights to develop, manufacture and commercialize a collection of early preclinical programs and compounds with potential application as novel antibiotics targeting gram-negative and gram-positive bacterial cell envelope enzymes. The company is focused on the discovery and development of antibiotic classes that target serious multidrug-resistant bacterial infections. Specific terms of the agreement were not disclosed.

Other news to note

Synergy Pharmaceuticals Inc., of New York, said the FDA has approved Trulance (plecanatide) 3-mg tablet for the once-daily treatment of irritable bowel syndrome with constipation in adults. This is the second indication for the product, which is already approved for the treatment of adults with chronic idiopathic constipation. With the exception of a single amino acid substitution for greater binding affinity, Trulance, the company said, is structurally identical to human uroguanylin and is the only treatment thought to replicate the pH-sensitive activity of uroguanylin. (See *BioWorld Today*, Jan. 23, 2017.)

Synpromics Ltd., of Edinburgh, Scotland, said it will work with the University College London Great Ormond Street Institute of Child Health to develop gene therapies for pathologies affecting the hematopoietic system. The objective of the work is to develop synthetic promoters that can be directly applied to gene-modified cell therapy, particularly where cells such as microglia or other myeloid cells can be used to deliver a therapeutic protein to the target pathologic sites, the company said. Output from the collaboration also has direct applications to further improve CAR T therapy, it added. Financial terms of the agreement were not disclosed.

Synthon NV, of Nijmegen, the Netherlands, gained FDA fast track status for its investigational anti-HER2 antibody-drug conjugate (ADC), [vic-]trastuzumab duocarmazine, also known as SYD-985. The designation is for treating patients diagnosed with HER2-positive metastatic breast cancer that has progressed during or after at least two HER2-targeting treatment regimens for locally advanced or metastatic disease, or progressed during or after [ado-]trastuzumab emtansine treatment. The company is currently enrolling the pivotal phase III trial, Tulip, a multicenter, open-label, randomized study comparing the efficacy and safety of the ADC to physician's choice treatment.

Topas Therapeutics GmbH, of Hamburg, Germany, said it will serve as the exclusive translational partner for the recently extended Collaborative Research Center (CRC) 841, which is focused on liver inflammation. The center has 25 subprojects investigating the causes and mechanisms of inflammatory liver diseases, laying the groundwork for new therapeutic approaches, the company said. CRCs are funded by the German Research Foundation (Deutsche Forschungsgemeinschaft). CRC 841, at the University Medical Center Hamburg-Eppendorf, has been funded by the DFG since 2010 and will now receive nearly €15 million (US\$18.7 million) for the third and final projects phase.

Xbiotech Inc., of Austin, Texas, highlighted the publication of "A Natural Human Monoclonal Antibody Targeting Staphylococcus Protein A Protects Against *Staphylococcus aureus* (*S. aureus*) Bacteremia." in *PLOS ONE*. The article reports on research involving the company's therapeutic monoclonal antibody, 514-G-3, and its ability to neutralize a key immune evasion mechanism of *S. aureus* involved in the establishment of serious infections. The company reported top-line results

from a phase I/II study of 514-G-3 in April 2017.

Zosano Pharma Corp., of Fremont, Calif., said shareholders approved an increase in the number of authorized company shares (NASDAQ:ZSAN) from 100 million to 250 million and a reverse stock split, in which the company's board has chosen a 1-for-20 ratio of exchange. Shares were due to begin trading on a split adjusted basis Friday. Shares of the company have ranged from a 52-week high of \$3.54 cents to a 52-week low of 37 cents reached Thursday.

Regulatory front

Drug and device companies may get some relief from unwarranted qui tam suits alleging that they violated the False Claims Act (FCA). In the past, the U.S. **Department of Justice** (DoJ) has declined to join defective or frivolous whistleblower suits alleging FDA violations. Now the DoJ is instructing its attorneys to go a step further and seek to dismiss such suits in the interest of saving time and resources. The DoJ recently issued an internal memo, made available by the FDA Law Blog, that includes a list of factors that could be grounds for seeking a dismissal. In addition to curbing frivolous or defective suits, the attorneys are encouraged to use the dismissal tool to prevent "parasitic or opportunistic qui tam actions" that duplicate pre-existing government investigations, prevent interference with agency actions and programs, protect DoJ litigation, safeguard classified information, preserve government resources and address egregious procedural errors.

The U.S. **Patent and Trademark Office** (PTO) is getting pushback against a new policy that makes applicants pick up the tab for PTO attorney fees, win or lose, in court challenges. The **American Bar Association** (ABA) filed an amicus brief this week with the **Federal Circuit**, arguing that a provision of U.S. patent law that holds applicants responsible for "all expenses" of a court action challenging a PTO administrative decision does not give the government the right to be reimbursed for its lawyers' expenses. "For nearly two centuries, the phrase 'all expenses of the proceedings' has been understood universally to mean that the applicant must pay only the PTO's out-of-pocket expenses for the proceedings, like travel costs and expert witness fees," the ABA brief said. "The PTO now urges a radical, novel departure from that longstanding interpretation." The change in policy could prevent applicants who lack the funding to cover the PTO's attorney fees from seeking a review of decisions made by the Patent Trial and Appeal Board, the ABA said. The amicus brief asked the Federal Circuit to reverse a 2-1 decision it made in *Nantkwest Inc. v. Joseph Matal*, in which it awarded the PTO nearly \$80,000 for attorney fees. The 2017 ruling reversed a district court decision that had awarded the PTO witness costs but not attorney fees. Holding to the "American Rule," the lower court said each party was responsible for its own attorney fees, even though **Nantkwest**, of Culver City, Calif., lost its bid to force the PTO to patent a claimed method of treating cancer by administering natural killer cells. The Federal Circuit agreed in August to rehear the case en banc.

In the clinic

Generon Corp., of Shanghai, reported that the first pivotal phase III study in the U.S. for F-627 (benegrastim) to treat chemotherapy-induced neutropenia in breast cancer patients met its primary endpoint. The primary endpoint was to shorten the duration in days of grade 4 neutropenia in the first chemotherapy cycle. Patients treated with F-627 demonstrated significantly reduced duration of severe neutropenia compared to patients in placebo group ($p < 0.0001$). F-627 is a recombinant human granulocyte colony-stimulating factor dimer. (See *BioWorld*, Oct. 18, 2017.)

GW Pharmaceuticals plc, of London, said results of its phase III trial testing Epidiolex (cannabidiol), a cannabinoid lacking euphoric side effects, in 171 patients with Lennox-Gastaut syndrome (LGS) were published in *The Lancet*. After a two-week dose-escalation period and 12 weeks of maintenance treatment, patients taking Epidiolex had a 44 percent median decrease in drop seizures compared to a 22 percent median reduction for patients taking placebo. An NDA for Epidiolex as a treatment for LGS and Dravet syndrome is currently under FDA review with a PDUFA goal date of June 27. (See *BioWorld*, Dec. 5, 2017.)

Iovance Biotherapeutics Inc., of San Carlos, Calif., reported preliminary data from two ongoing phase II trials testing its autologous tumor infiltrating lymphocytes LN-145. In the C-145-03 trial testing the drug in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck, LN-145 produced a reduction of tumor size of at least 30 percent in three of eight patients. The trial continues to enroll patients up to the expected 47 patients. In the C-145-04 trial, there was one partial response and one patient with stable disease among two currently evaluable patients with recurrent, metastatic or persistent cervical carcinoma treated with LN-145.

Novan Inc., of Morrisville, N.C., treated the first patient in a phase II trial testing its topical nitric oxide product candidate, SB-206, for the treatment of molluscum contagiosum. The trial, which is scheduled to enroll 192 children and adolescents with an option to increase the enrollment to 256 patients, will test three concentrations of SB-206 compared to vehicle, measuring the proportion of patients achieving complete clearance of all molluscum lesions at week 12. Top-line data from the trial are expected in the fourth quarter.

Orphazyme A/S, of Copenhagen, said results from its phase II trial testing arimoclomol in patients with SOD1 amyotrophic lateral sclerosis (ALS) were published in *Neurology*. The drug was deemed safe and well-tolerated at a dosage of 200 mg three times a day for up to 12 months. Secondary endpoints, including survival, function based on ALS Functional Rating Scale Revised scores, vital capacity, and the combined assessment of function and survival, all favored arimoclomol although they weren't powered to demonstrate efficacy. Orphazyme plans to start a phase II/III registration trial for arimoclomol in patients with ALS in the second half of 2018.

Rexgenero Ltd., of London, treated the first patient in its phase III program testing REX-001, an autologous cell therapy,

in patients with critical limb ischemia (CLI) and diabetes mellitus. The program consists of two trials, one in patients with Rutherford stage 4 CLI that will assess complete relief of ischemic rest pain and a second in patients with Rutherford stage 5 CLI that will measure complete ulcer healing. Both trials, which will enroll a total of 138 patients, will measure amputation-free survival as a secondary endpoint. Interim results are anticipated in about 18 months with full data expected in 2020.

Takeda Pharmaceutical Co. Ltd., of Osaka, Japan, and **Zinfandel Pharmaceuticals Inc.**, of Chapel Hill, N.C., terminated the phase III TOMMORROW trial after a planned interim futility analysis showed an inadequate treatment effect for pioglitazone 0.8 mg SR in delaying the onset of mild cognitive impairment due to Alzheimer's disease. The companies plan to present the data at a future scientific meeting.

TFS Trial Form International AB, of Lund, Sweden, said that Grifols SA subsidiary **Araclon Biotech SL**, of Zaragoza, Spain, has decided to continue to advance the Alzheimer's disease (AD) vaccine ABvac-40 into phase II. The placebo-controlled trial will be carried out at 21 clinical investigational sites across Europe over the next two years. The trial, approved by the Spanish Agency of Medicinal Products and Medicinal Devices, will enroll 120 participants. Some will have amnesic mild cognitive impairment and some will have very mild AD, in order to evaluate the efficacy and safety at early stages of the disease, both at the cognitive and molecular levels, TFS said.

The Medicines Co., of Parsippany, N.J., completed enrollment of more than 1,500 patients with atherosclerotic cardiovascular disease (ASCVD) or cardiovascular risk-equivalents in the phase III ORION-11 trial testing inclisiran. The trial will measure the LDL-C reduction from baseline to day 510 as the primary endpoint. Two other phase III trials, ORION-9 in heterozygous familial hypercholesterolemia and ORION-10 in ASCVD, are on schedule to complete enrollment during the first half of 2018. The company also noted that the FDA granted orphan drug designation to inclisiran for the treatment of homozygous familial hypercholesterolemia (HoFH). A phase III trial in patients with HoFH is scheduled to begin in 2018. Inclisiran, an RNAi targeting PCSK9, was discovered by Cambridge, Mass.-based **Alnylam Pharmaceuticals Inc.**

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Regulatory front

Endo International plc, of Dublin, agreed to an **FDA** request to seek a temporary stay of a lawsuit its subsidiaries Par Sterile Products LLC and Endo Par Innovation Co. LLC filed in October over the agency's interim policy on compounding using bulk drug substances. The suit claimed the policy violated the 2013 Drug Quality and Security Act (DQSA); it also sought the immediate removal of vasopressin from FDA's Category 1 nominations list to assure that outsourcing facilities can't compound vasopressin-containing drugs in bulk. The agreement followed the agency's public statements last week that it planned to alter its compounding policy to comply with the DQSA. The stay will be in effect until March 30, by which time the FDA plans to provide more details on how it will change its compounding policy to comply with the DQSA and ensure that outsourcing facilities do not compound using a bulk drug substance when an FDA-approved drug can be used to meet patient needs.

As a result of its review of existing regulations, the **FDA** is issuing a direct final rule and a companion proposed rule to provide more flexibility for its biologics inspections. The rule revises the time of inspection requirements in 21 CFR 600.21 and removes the duties of inspectors required under 21 CFR 600.22. "These changes to the biological product regulations eliminate outdated requirements and accommodate new approaches, such as a risk-based inspection frequency . . . thereby providing flexibility without diminishing public health protections," the FDA said in a notice scheduled for publication

in Friday's *Federal Register*. The revision will not change the biological product establishment inspection requirements and investigator duties included in sections 704 and 510(h) of the Federal Food, Drug and Cosmetic Act. The *Federal Register* publication will kick off a 75-day comment period. If the FDA receives no significant negative comments, the rule will go into effect 60 days later.

The **FDA** released a draft guidance Thursday to help sponsors develop fixed-dose combination drugs to treat hypertension. The guidance focuses on the clinical development of two-drug combinations of previously approved drugs. The comment period on the draft will be open for 60 days.

The **FDA** is reminding sponsors of brand and generic systemic antibacterial and antifungal drugs that the clock is ticking on when they have to meet the new labeling requirements for susceptibility test interpretive criteria. In accordance with the 21st Century Cures Act, the FDA established a website Dec. 13 that contains a list of new and updated susceptibility test interpretive criteria and standards. Sponsors of approved brand and generic drugs listed on the website have one year from the time the site went up to remove the current susceptibility test interpretive criteria information from their labeling and replace it with a reference to the FDA's Interpretive Criteria Website.

The **U.N.'s 40th Expert Committee on Drug Dependence** will meet in May for a pre-review of cannabis and its major components, according to an **FDA** notice slated for publication in Friday's *Federal Register*. Cannabidiol, which is produced for pharmaceutical purposes as a cannabis extract, will be subject to critical review at the meeting.

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