Illumina aims at a more comprehensive sequencing offering with the acquisition of PacBio

BY KELSEY KAUSTINEN
SAN DIEGO & MENLO PARK, Calif.— illumina Inc. is going to face the coming new year with new growth, having announced an agreement under which it will acquire Pacific Biosciences for $8 per share in an all-cash transaction. Both companies’ boards of directors have approved the deal, which has a total enterprise value of roughly $1.2 billion on a fully diluted basis.

That price represents a 71-percent premium over PacBio’s 90-day trading volume weighted average share price as of Oct. 31, the day before the transaction was made public. The acquisition is expected to close by mid-2019, pending shareholder approval on the part of Pacific Biosciences, regulatory approval and other customary closing conditions.

As noted by Francis deSouza, president and CEO of illumina, this is the company’s largest acquisition since it absorbed Solexa in 2007.

“The decade since our acquisition of Solexa, illumina’s short read SBS-based technology has transformed the landscape of genomics with the delivery of large-scale and increasingly economical sequencing,” deSouza commented in a conference call. “Illumina’s SBS technologies have played

Illumina (pictured here) is on track to acquire Pacific Biosciences—also known as PacBio—for more than $1 billion to expand its sequencing offerings.

Innovate looking for answers about NASH

Company studies the effects of larazotide on nonalcoholic fatty liver disease

BY JENNIFER CLIFFORD
RALEIGH, N.C.—This fall, Innovate Biopharmaceuticals Inc., a clinical-stage biotechnology company focused on developing novel therapeutics for autoimmune and inflammatory diseases, announced the possibility that its lead agent, larazotide acetate, may have the potential to be used in conjunction with other drugs to treat nonalcoholic steatohepatitis (NASH).

In a recent study, researchers assessed the effects of multiple doses of larazotide on various markers of NASH in a preclinical model called the DIAMOND mouse model. Researchers also kept an eye on the effects of larazotide on gut integrity, using a highly specific technique measuring epithelial barrier normalization and intestinal permeability. Agents that can prevent gut barrier permeability, or a “leaky” barrier, from worsening with the progression of NASH could pose a significant advantage in treating this disease.

Preclinical data showed in high numbers that specific technique measuring epithelial barrier permeability could pose a significant advantage in treating this disease. In the organ. In the United States, NASH

Innovate Biopharmaceuticals’ preclinical experiments suggest that larazotide acetate may have the potential to be used in conjunction with other drugs to treat the liver disease nonalcoholic steatohepatitis—agents like this one that can prevent gut barrier permeability could pose a significant advantage in treating this disease.

liver diseases, specifically NASH. NASH is a severe disease of the liver caused by inflammation and a buildup of fat in the organ. In the United States, NASH

INNOVATE CONTINUED ON PAGE 18
With hundreds of known cancer types and a steady increase in the incidence of cancer worldwide, researchers need a diverse range of innovative technologies to help unravel the complexities of the disease. Our cancer research solutions support your research and discovery, wherever it leads – from genomics to cell-based analysis to animal and tissue imaging – and can help you translate your findings into more effective treatments. Cancer is a complex story – and now you have the tools to help you understand it.

Learn more at www.perkinelmer.com/cancer-research
GlobalData shares insights on likely arcs of various therapeutic arenas

BY JEFFREY BOULEY

LONDON—Data and analytics company GlobalData has shared its predictions recently on the growth trajectories of several markets for pharma and biotech therapeutics, and we will share them all with you momentarily. But we will begin with the liver, because far and away the most dramatic potential is in the size of the non-alcoholic steatohepatitis (NASH) market across the seven major markets (7MM) of the United States, Germany, France, Italy, Spain, United Kingdom and Japan—a stunning 54 percent increase over the next 10 years, rising from $1.8 billion in 2017 to $48 billion in 2027 at a CAGR of 10.3 percent.

Certainly, we here at DDNews have noticed the spate of news on NASH from the discovery level all the way up to the clinical trial level, and GlobalData’s report “Non-Alcoholic Steatohepatitis (NASH): Dynamic Market Forecast to 2026” details the most recent round of developments in the treatment landscape of NASH.

GlobalData also found that there is opportunity in the NASH space for companies which can develop combination therapies for the disease, with Moore noting that key opinion leaders who spoke with GlobalData expressed the belief that using combination therapies to tackle NASH was a viable strategy and would be well received by physicians and payers across the 7MM.

He added: “Theoretically, many of the drugs currently in development for NASH have complementary mechanisms of action, and would work well when used concomitantly with each other. However, for many companies in the NASH space, producing a combination therapy would require collaboration with competitors, which could be a major barrier to this strategy.”

Opioid use disorder market

Another recent GlobalData report predicts that the opioid use disorder market should experience solid growth over the next 10 years, rising from $1.8 billion in 2017 to $4.8 billion in 2027 at a CAGR of 10.3 percent.

Current treatments are based around maintenance therapy with an opioid agonist, buprenorphine and methadone, or an opioid antagonist, naltrexone. In the case of an overdose, naloxone can be used as an acute rescue medication, and in some cases it is used in combination with buprenorphine.

“NASH is a common and prevalent disease, and many patients who have cirrhosis are at risk of developing NASH due to liver transplants. Furthermore, unlike in non-cirrhotic NASH patients, the current treatment guidelines for NASH do not recommend the use of any off-label therapies in patients with cirrhosis,” Moore continued. “Consequently, this patient segment carries the greatest unmet need for new treatments, which will drive rapid uptake of any drug which launches targeting these patients.”

GlobalData is predicting growth in several therapeutic markets, but the most dramatic growth by far is likely in the area of developing treatments for the liver disease non-alcoholic steatohepatitis.

A look at the markets

GlobalData is predicting growth in several therapeutic markets, but the most dramatic growth by far is likely in the area of developing treatments for the liver disease non-alcoholic steatohepatitis.

MARKETS CONTINUED ON PAGE 4

Genetic disease company snaps up $90M in financing

Stoke Therapeutics leads our latest roundup of financing rounds in pharma and biotech

BY JEFFREY BOULEY

BEDFORD, Mass.—We have a few companies to look at in our tour through the most notable news to hit my inbox about financing rounds from late October through late November, but we will start with the oldest of those bits of news, because it is the biggest momentarily: Stoke Therapeutics completed in October a $90 million Series B financing to advance its pipeline of antisense oligonucleotide medicines for NASH syndrome and other severe genetic diseases.

The financing round was led by RTW Investments with participation from founding investor Apple Tree Partners. New investors include RA Capital Management, Cormorant Asset Management, Perceptive Advisors, funds managed by Janus Henderson Investors, Redmile Group, Sphera Funds Management and Alexandria Venture Investments.

Stoke says it has identified thousands of genes that could be addressed by its proprietary TANGO technology, which targets non-protein RNA splicing to increase gene expression and address the root cause of monogenic diseases caused by loss or reduction of gene function. The company is advancing its lead program, a therapeutic candidate for Dravet syndrome, and expects to be in the clinic by early 2020. Stoke has also built a pipeline of candidates targeting other diseases of the central nervous system, as well as diseases of the eye, ear, liver and kidney.

“Our technology is designed to address, for the first time, the genetic cause of diseases like Dravet syndrome so we can do more than alleviate symptoms—we can potentially prevent the long-term disabling consequences of these diseases,” said Dr. Edward M. Kaye, CEO of Stoke Therapeutics. “We are delighted to have the support of such an outstanding group of crossover investors to speed our progress toward the clinic.”

“We are delighted to have the support of such an outstanding group of crossover investors to speed our progress toward the clinic.”

Stoke Therapeutics, with its innovative scientific approach, strong preclinical data and seasoned leadership team, is well positioned to be a leader in oligonucleotide therapeutics,” said Dr. Roderick Wong, managing partner and chief investment officer at RTW Investments.

“Rare disease patients are waiting, and we look forward to supporting Stoke as it builds a great precision medicine company advancing disease-modifying programs into the clinic.”

89Bio launches into liver and metabolic disorders

SAN FRANCISCO & HERZLIYA, Israel—89Bio, a clinical-stage biopharmaceutical company focused on nonalcoholic steatohepatitis (NASH) and other liver and metabolic disorders, announced in October that it had closed a $60 million Series A financing. The funding will be used to advance the company’s pipeline of biologic and small-molecule drug candidates acquired from Teva Pharmaceutical Industries Ltd. The investment round was led by Orbimed Israel, Orbimed US and Longitude Capital and joined by RA Capital Management and Pontifax. Orbimed Israel and Orbimed US founded 89Bio.

89Bio’s lead candidate for the treatment of NASH is BIO89-100 (formerly TEV-47948). Currently in Phase 1, BIO89-100 is a novel long-acting glycopegylated fibroblast growth factor 21 (FGF21) analog that was developed using a proprietary glycopegulation technology to prolong the half-life and optimize the biological activity of native FGF21. In preclinical studies, BIO89-100 demonstrated a long half-life, potentially enabling extended-interval dosing, and significant improvements in biomarkers such as body weight, blood glucose and lipids. 89Bio also has an undisclosed preclinical candidate with potential utility in other related disorders.

“NASH is a common and complex multifactorial disease

FINANCE CONTINUED ON PAGE 4
**MARKETS**

**Continued from page 3**

with buprenorphine. Key opinion leaders have stated that these treatments provide adequate cover for opioid-naive patients, which means the main unmet needs in the field are environmental, such as improving treatment access for those addicted to opioids and improving physician prescribing habits to staunch the flow of opi- oids to the public.

“There are two distinct strategies in the pipeline, and they can be neatly divided into late-stage strategy and early-stage strategies,” said Marco Mucciaro, director of neurology and ophthalmology at GlobalData. “The late-stage focuses on reformulations of currently marketed drugs, so the route of administra- tion is more favorable to patients. In con- trast, the early-stage strategies focus on novel mechanisms of action, aimed at targeting the root cause of addiction.”

“Any new drug which is proven to help patients with NASH is expected to see rapid uptake, and generate significant market growth.”

Dr. Thomas Moore of GlobalData

**Lung cancer market**

There has been a recent spate of approvals in both small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), notes GlobalData, but there is a stark difference in the growth arcs for the two segments—GlobalData expects the global NSCLC market to be worth $146.6 billion by 2024, which is sixfold more than the SCLC market, which is expected to reach only $2.5 billion in the same timeframe.

But this growth also poses complexities in the clinical setting, with Francesca Blum, UK oncology director at GlobalData, noting: “As SCLC and NSCLC both have more than 20 immunotherapy products currently in Phase 2 or 3 development, treatment paradigms for both forms of the disease will become increasingly complex, requiring treatments to be chosen from a growing selection of similar options.”

Alongside the much-needed increase of targeted treatment options for NSCLC patients with ALK or EGFR mutations, the use of immuno-oncology is also expanding, particularly into subtypes of lung cancer with significant unmet needs, GlobalData says.

**Glioblastoma market**

Moving from lung cancer to brain cancer, the glioblastoma (GBM) market is expected to grow from $662 million in 2017 to $1.4 billion in 2027 across the 7MM, at a CAGR of 1.8 percent, according to GlobalData.

“The modest growth of the CLL market will be driven by increasing incidence, primarily by aging populations, as well as label expansions into the first-line setting for AbbVie/Roche’s Venetexlsta,” frontline approval of the combination of AbbVie/John- son & Johnson’s Imbruvica + Venetexlsta, and the increasing use of combination therapies instead of monotherapies or chemotherapy combination therapies,” according to GlobalData’s Blum. “Non-toxic therapies that have a fixed duration of therapy are expected to play an increasingly large role in the CLL market, which can be achieved using combinations of targeted drugs.”

Generic and biosimilar erosion of some of the mainstays of CLL treatment is also expected during the forecast period. “A major barrier for market growth in CLL will be the increased use of rituximab biosimilars and generic ibritinib, which will erode sales of current standards of care Rituxan and Imbruvica,” Blum added. “In addition, novel targeted agents such as AstraZeneca’s Calquence (acalabrutinib) and TG Therapeu- tics’ umbralisib will enter the market during the forecast period, but overall, there’s a lack of innovative drugs in the late-stage pipeline with novel mechanisms of action, means that next-generation agents are not expected to generate significant sales.”

GlobalData’s report also found that novel research and development strategies are being investigated in early-stage clinical tri- als for the treatment of CLL.

Blum concluded: “Several immunothera- pies are in early-stage development, primarily checkpoint inhibitors and chimeric antigen receptor T cell therapies, so in future, CLL may also be treatable with immuno-oncolo- gy regimens, as is already the case for other hematological malignancies such as acute lymphocytic leukemia and diffuse large B cell lymphoma.”

**FINANCE**

**Continued from page 3**

linked to obesity and type 2 diabetes for which there are no approved treatments,” said Dr. Arun Sanyal, a professor of gastro- enterology and hepatology at the Virginia Commonwealth University. “FGF21 is a compelling target for intervention. Given its metabolic role across multiple organs, Bio89-100 has the potential of affecting the disease pathway in both metabolic and fibrosis endpoints.”

**Forbion invests €12.5M in OMEICOS**

NAARDEN, The Netherlands & MUNICH—In early November, European life-sciences venture capital firm Forbion announced that it had led a €17.9 million (about $20.3 million) Series C financing of OMEI- COS Therapeutics GmbH, a privately held biopharmaceutical company based in Berlin. Forbion was the only new investor participating in the financing round, contributing €12.5 million from its recently launched Forbion IV Fund. Existing OMEICOS investors Vesalius Bio- capital II S.A., SICAR, Rensselaer BioPharma Fund, SMS Group GmbH, KFW Group, VC Fonds Technologie Berlin, High-Tech Gründerfonds and The Falk Reversible Trust participated in the financing.

OMEICOS is developing first-in-class small-molecule therapeutics that are metabolically robust, synthetic analogs of epoxyeicosanoids, for the prevention and treatment of cardiovascular and oph- thalmic diseases. Epoxyeicosanoids are naturally occurring, but metabolically unstable, metabolites of omega-3 fatty acids that can activate anti-inflammatory, anti-arrhythmic and cardioprotective pathways in heart cells. The company’s synthetic version can be administered orally and has reportedly shown improved biological activity and pharmacokinetic properties compared to its natural counterparts.

In July, OMEICOS announced that a Phase 1 safety and tolerability study for its lead compound, OMT-28, designed for the treatment of atrial fibrillation, met its primary endpoint and that it intends to accelerate initiation of a Phase 2 trial.

**Intensity Therapeutics raises $6.5M**

WESTPORT, Conn.—Intensity Therapeu- tics Inc., a clinical-stage biotechnology company developing proprietary immune cell-activating cancer treatments, in November announced the completion of a $6.5 million Series B financing.

Intensity plans to use the proceeds of the financing to advance the clinical development of lead product candidate INT330-6, a direct intratumoral injec- tion that is currently being evaluated in a Phase 1/2 clinical study in patients with various advanced solid tumors. The company intends to expand the study by adding clinical sites outside the United States and Canada, as well as adding combination arms with an anti-PD-1 antibody.
Covering the News of Pharma, Biotech & Life Science

YOUR REGULAR DOSAGE OF NEWS IN THE AREAS OF:

- DISCOVERY
- RESEARCH & DEVELOPMENT
- PRECLINICAL
- CLINICAL TRIALS
- DIAGNOSTICS
- CONTRACT SERVICES
- BUSINESS & GOVERNMENT POLICY

For the pharma, biotech and life-sciences professional, understanding the complex process that results in new marketed therapeutics is an on-going challenge. In DDNews, you get insightful reporting and analysis of each stage in the pipeline—in print and online—from a staff of experienced life-science journalists. It’s an information resource you can’t find anywhere else.

Are there important issues, research areas or technologies you would like to read more about in DDNews?

Let us know at Twitter (@DDNewsOnline) or friend us on Facebook.
VIB taps Biomatters for cloud-based software solution

AUCKLAND, New Zealand—The VIB, a life-sciences company discovering and developing novel medicines, has selected Biomatters’ Geneious Biologics software solution to consolidate and manage our sequence data in a cloud-based software solution that provides powerful, fast and deep analytics to support therapeutic biologics discovery. The software supports the analysis of antibodies and related constructs using DNA sequence data, and uses visualization tools and advanced analytics to help users identify new therapeutic candidates.

“Geneious Biologics will help us scale-up our screening efforts. We are incorporating more high-throughput sequencing into our core business, and are screening increasingly large quantities of unique and complex VH-HH-based multi-specific antibodies. We sought a bioinformatics platform that provides powerful, fast and deep sequence analysis and, importantly, allows us to consolidate and manage our sequence data in a secure environment that can be shared with our partners,” said Bruno Dombrecht, expert scientist at VIB Discovery Sciences.

Sitryx and Sygnature join hands to develop therapeutics in immuno-oncology and immuno-inflammation

Oxford, U.K.—Targeted toward discovering how the body’s own immune system can be tweaked to fight cancer, Sitryx Therapeutics Ltd., a biopharmaceutical company focused on regulating cell metabolism, is collaborating with Nottingham, U.K.-based contract research organization Sygnature Discovery Ltd. to develop disease-modifying therapeutics in immuno-oncology and immuno-inflammation.

“Sitryx is focused on regulating cell metabolism, is well placed to identify potential druggable targets for the development of new therapies to treat cancer and inflammation, Weir says. Sitryx supports the key hypothesis that it is possible to manipulate intracellular metabolic pathways in specific cells to alter their activity and attempt to defeat disease.

“We are pleased to have been selected by Sitryx to support their groundbreaking research efforts to develop disease-modifying therapeutics across multiple biological targets in immuno-oncology and immuno-inflammation,” says Sygnature’s CEO and founder, Dr. Simon Hirst. “Our considerable in-house knowledge of immuno-oncology and immuno-inflammation discovery will enable us to efficiently navigate these complex areas of biology to support the identification and development of new therapies to treat cancer and inflammation. Weir says. Sitryx scientists are exploring multiple metabolic pathways within immune cells to identify potential druggable targets for the development of new therapies to treat cancer and inflammation. Pictured here is a tumor being attacked by T cells.
IMMUNO
CONTINUED FROM PAGE 6

optimalization of novel and selective small molecules, while developing a deep understanding of their mode of action.”

The role of cancer metabolism has been shown to be pivotal in controlling the behavior of disease associated cells in immunology and immunology-inflammation, according to Sygnature. Correcting immune cell function and/or inhibiting tumor cell growth through targeting metabolic pathways has the potential to deliver new complementary and highly differentiated approaches to treat a wide range of severe diseases.

Weir says that ideally, some of the newly discovered therapies could be used in addition to chemotherapy and other drugs to treat cancer patients, while other therapies might be designed to replace the challenging treatment of severe diseases.

Rather than killing cancer cells from outside of the body, the immune cells would be manipulated to treat cancer from the inside, using the body’s own immune system, he says.

Private equity-backed since 2017, Sygnature operates research facilities in Nottingham and Alderley Park, U.K., housing over 200 research scientists. The company says its “drug hunters” have the know-how required to undertake the most demanding of research programs and drive them from target validation through hit identification, hit-to-lead and lead optimization to preclinical development. Since 2011, Sygnature says it has delivered 14 drug candidates to clients which have subsequently entered Phase 1 and 2 clinical trials.

Sygnature set the stage for the Sygnature collaboration with the announcement on Oct. 8 of the closing of its Series A financing round. Founded with seed funding from SV Health investors, Sygnature raised $30 million from a syndicate of specialist international healthcare investors co-led by SV Health Investors, Sofinnova Partners, the Longwood Fund and the global healthcare company, GlaxoSmithKline (GSK).

Immunometabolism is also a fast-emerging area of investigation into the role of metabolic pathways in immune cell function. Changes to these pathways have been shown to be pivotal in the development of a number of severe diseases, including a range of cancers and autoimmune conditions.

Correcting immune cell function and/or inhibiting tumor cell growth through immunometabolic therapies have the potential to be key, complementary and highly differentiated approaches to treating disease, Weir says.

Sygnature consults the world-leading scientists, deep biological insights and world of immunometabolism to address a broad range of immunometabolic targets, he notes. Through differentiated chemistry approach and/or targeting chimera (PROTACS) and topical formulations—Sygnature has built a portfolio of projects addressing oncology and immunometabolic indications.

Sygnature’s proprietary science is supported by GSK’s drug discovery and chemistry experts, as well as having access to certain GSK technologies and the licensing of intellectual property, including chemical matter.

GSK’s interest in Sygnature arose from work within the Immunology Network, a unique open collaboration initiative connecting GSK to the work of academic scientists and their novel immunology research, Weir explains.

Sygnature was co-founded by a team of world-leading scientists from the United States and Europe, who have contributed significantly to the field, Weir says. This includes Reza Ashrafian, partner at SV Health Investors; Luke O’Neill, professor of biochemistry, School of Biochemistry and Immunology at Trinity College Dublin; Jonathan Powell, professor of oncology and associate director, Institute for Cancer Immunotherapy, Johns Hopkins University and Paul Peter Tak, former chief immunology officer and senior vice president at GSK, and professor of medicine at Amsterdam University Medical Centre.

“Immunometabolism is an extremely exciting and compelling scientific area and, at Sygnature, we have seen that modulation of these key cellular pathways has broad therapeutic potential across multiple disorders with unmet medical needs,” Weir said in October. “Together with our proprietary chemistry, deep biological insights and world-class expert in immunometabolism experts, Sygnature is well positioned to become a leader in immunometabolism.”

John Lepore, senior vice president of research at GSK, said: “Immunology is at the heart of GSK’s new approach to R&D. Through our Immunology Network, we believe the emerging field of immunometabolism that Sygnature is focusing on has the potential to bring new therapeutic opportunities to patients for a broad range of diseases including cancer.

“Our investment in Sygnature will allow us to access this exciting science through working closely with world-renowned academic scientists in an open, collaborative way,” said Lepore.

AMPK
CONTINUED FROM PAGE 1

other kinds of tumors to grow. The lab of Salk professor Dr. Reuben Shaw studied mice with and without the AMPK regulator to see how tumors developed. Their findings, recently published in the journal Cell Metabolism, suggest promising potential for targeted activation or deactivation of AMPK in different cancer types.

AMPK plays a key role as a master regulator of cellular energy homeostasis. It is a fuel-sensing enzyme that is activated in response to stresses that deplete cellular adenosine triphosphate (ATP) supplies such as low glucose, hypoxia, ischemia and heat shock. Because mutant tumor cells are able to steal energy in order to grow, their presence can activate AMPK and trigger processes that slow its growth. AMPK can both increase ATP generation such as fatty-acid oxidation and glucose transport, and decrease others that consume ATP, but are not acutely required for survival, such as lipid and protein synthesis and cell growth and proliferation—inhbiting the tumor and helping to restore other normal cellular functions. The recent findings at Dr. Shaw’s lab, however, also found that the presence of AMPK could help larger existing tumors to grow.

“Our study shows that the same dysfunction in a genetic circuit that causes non-small cell lung cancer to begin with is necessary for more mature tumor cells to survive when they don’t have enough nutrients,” says Shaw, director of the Salk Cancer Center and the paper’s senior author. “It’s exciting because not only does it solve a genetic ‘whodunnit,’ but it also points to a potential new therapeutic target for a cancer that is often diagnosed very late.”

In studying the mice, they observed how tumors developed and progressed in mice with AMPK, and others without, and which genes from the same mouse were being activated under differing conditions. They noticed that when a tumor reached a certain size, AMPK actually stimulated a gene (Tie3) responsible for recruiting cellular materials and creating them—when interior cells could no longer access the needed energy to grow, AMPK signaled Tie3 to cannibalize pieces of the cell so the tumor could grow.

“We found that tumors grew much more slowly when AMPK was not present. That means that AMPK is not always functioning as a tumor suppressor, as we originally thought. Previously, we were focused on how we could activate AMPK. Now that we’ve identified this mechanism, we can shift to how to inhibit it in certain cancers.”

Dr. Lillian Eichner of the Salk Institute

“Showen here are genetically engineered lung tumors (solid purple) within the native lung environment.”

“Showen here are genetically engineered lung tumors (solid purple) within the native lung environment.”

“Showen here are genetically engineered lung tumors (solid purple) within the native lung environment.”

“Showen here are genetically engineered lung tumors (solid purple) within the native lung environment.”

For more information, visit www.DDN-News.com
Novo Seeds incubatee Embark Biotech enters collaboration with Novo Nordisk

**Novo Seeds incubatee Embark Biotech enters collaboration with Novo Nordisk**

**BY DDNEWS STAFF**

COPENHAGEN, Denmark—Novo Seeds, the early-stage investment arm of Novo Nordisk, wholly owned by the Novo Nordisk Foundation, announced in early November that its incubatee company Embark Biotech ApS has entered into a research collaboration with Novo Nordisk A/S focusing on the discovery of novel treatments for obesity and its associated metabolic pathologies through mechanisms that increase energy expenditure.

The aim of the collaboration is to develop novel drug candidates that help people with obesity lose weight by burning off excess energy instead of storing it as fat.

Embark was first incubated by Novo Seeds in 2016 as a spinout from the Center for Basic Metabolic Research at University of Copenhagen, based on a pre-seed grant program from the Novo Nordisk Foundation. Co-founder and CEO Casper Tind Hansen, who was instrumental in the creation of the company and its research platform, also serves as an entrepreneur in residence at BiOrigin, a recently established advisory unit for Novo Seeds.

Our financial engagement in Embark demonstrates how our team can successfully translate strong academic discoveries into innovative start-up companies,” said Emmanuelle Costeau, a partner at Novo Seeds. “This collaboration with Novo Nordisk has the potential to develop next-generation anti-obesity therapies that will significantly improve the quality of life for patients.

“In addition to funding, we bring our commercial expertise to provide strategic support to portfolio companies, steering them through the critical start-up phase. As co-founder of Embark, Casper’s experience in establishing and managing early-stage companies has proven to be a valuable addition to our advisory unit, as we build our portfolio companies like Embark into successful biotech start-ups.”

Hansen, in turn, added: “Building on our academic founders’ insight and research into energy expenditure, we are thankful for the continued support from Novo Seeds, which has been instrumental in creating the Embark research platform and driving value creation through this collaboration with Novo Nordisk.”

The research platform of Embark builds on novel and unique insights into receptors that stimulate energy expenditure without triggering the sympathetic nervous system (the ‘light-or-flight’ response). The potential addition of energy expenditure drugs would make a meaningful difference in the treatment of obesity. As part of the collaboration agreement, Embark will receive research support for activities conducted in the collaboration, and Novo Nordisk has an option to license exclusive worldwide rights to develop and commercialize products discovered in the collaboration.

**TRPV6 CONTINUED FROM PAGE 6**

 investors and various programs from the governments of Canada and New Brunswick, asserts that its drug candidates have demonstrated a capability to reduce cancer cell viability, induce apoptosis and to reduce human tumor volume while minimizing side effects in classic animal and in vivo tumor models.

The journal article, “Inhibition of Transient Receptor Potential Vanilloid 6 Channel (TRPV6), Elevated in Human Ovarian Cancers, Reduces Tumor Growth in a Xenograft Model,” provides further support for the importance of TRPV6 in ovarian cancer. This calcium channel is the target for Soricimed’s anticancer drug candidates, and in the paper, the company demonstrates that the genetic message (mRNA) for TRPV6 protein and TRPV6 protein itself are greatly elevated in biopsies of all five types of ovarian cancer, at all stages. This is consistent with what has been reported for other solid tumor cancers, such as in the prostate or breast.

“We also show targeting TRPV6 with our lead drug candidate SOR-C13 inhibits ovarian tumor growth in animal models,” said corresponding author Prof. Jack Stewart, co-founder and chief scientific officer of Soricimed. “The conclusion from this work is that TRPV6 is a relevant therapeutic target for this difficult to treat disease.”

He added, “The role of TRPV6 in prostate and breast cancers is well documented, since it was first noted in 2002. TRPV6’s role in ovarian cancers that we report in this publication hadn’t been studied extensively until now. It is difficult to introduce a new cancer target to the oncology community but, in this case, the weight of evidence makes it quite clear that TRPV6 plays a key role in cancer pathogenesis. In addition, new data coming out indicating that ductal pancreatic cancer has also joined the TRPV6-rich cancer group.”

Soricimed also announced positive results demonstrating safety, tolerability and potential activity in a multicenter Phase I trial of SOR-C13 in patients who had advanced solid tumor cancers. SOR-C13 has been granted Orphan Drug status by the U.S. Food and Drug Administration for treatment of ovarian and pancreatic cancer.

Stewart discovered that the Northern short-tailed shrew is the only known mammal in North America that secretes a paralytic venom. After the discovery, he and his colleagues were the first to purify, characterize and synthesize this paralytic toxin, a unique peptide that inhibits sodium channels in nerves and offers potential for non-opioid pain treatment. Stewart named this protein soricidin, and Soricimed Biopharma was born. Further research on soricidin brought Stewart and his colleagues to the identification of two unique biological functions within the peptide—one domain that is paralytic and a second domain that is anticancerous. Stewart discovered that the target of the anticancer activity of soricidin was the calcium ion channel known as TRPV6. Solid tumor cancers produce large amounts of this channel. Because it plays a major role in cancer cell growth, proliferation and metastases, the channel represents a compelling target for the development of new cancer treatments.

Additional characterization of the anticancer domain of soricidin culminated in the identification of a subset of small peptides that are highly selective inhibitors of TRPV6 and candidates for development as anticancer therapeutics.

“TRPV6’s role in ovarian cancers ... hadn’t been studied extensively until now. It is difficult to introduce a new cancer target to the oncology community but, in this case, the weight of evidence makes it quite clear that TRPV6 plays a key role in cancer pathogenesis.”

Prof. Jack Stewart, chief scientific officer of Soricimed

TRPV6, one of approximately 33 ion channels in the super-family of TRP channels, is selective for calcium ion and is constitutively active. Its major function is uptake of calcium into the body through the gut. TRPV6 is now recognized as an oncogene and its gene classified as an oncogene or proto-oncogene, according to Stewart.

High expression of TRPV6 in breast cancer is consistent with pathological parameters and poor patient outcomes. Elevated TRPV6 has also been reported in estrogen receptor-negative breast cancers and correlated with poor prognosis for patients. All five types of ovarian cancer show similar elevated levels of both TRPV6 mRNA and protein. Over-expression of TRPV6 results in sustained elevation of calcium within the cancer cell, leading to cell proliferation and metastasis and inhibition of programmed cell death.

Stewart summarized, “Soricimed is the first company to develop a specific inhibitor of TRPV6 and to take it into clinical development as a potential treatment for solid-tumor cancers. Although the precise details of the TRPV6 pathway in cancer remain to be fully elucidated, a viable model does exists and is based on increased intracellular calcium resulting from the over-expression of TRPV6.”

EDITCONNECT: E121805
PARK2
CONTINUED FROM PAGE 6

from patients with the PARK2 gene associated with Parkinson's disease. It was also found that apoptosis of dopaminergic neurons derived from Parkinson's disease patients could be reduced by inhibiting calcium influx via T-type calcium channels.

From these results, it is suggested that combining disease-specific iPS cells and existing drug libraries has potential for both the development of treatments and clarification of disease pathology. The results of this research were published in the online version of Stem Cell Reports on Oct. 18.

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease, and causes motor symptoms such as tremor, bradykinesia, rigidity and postural instability and autonomic dysfunction due to a preferential loss of dopaminergic neurons in the substantia nigra. For 90 percent of Parkinson's disease patients, symptoms are idiopathic and it is difficult to understand the relationship between various factors, including those associated with the environment and the disease mechanism. However, approximately 10 percent of patients show the familial incidence of Parkinson's disease; as such, understanding the disease mechanism for familial Parkinson's disease may also link with the understanding of idiopathic Parkinson's disease as well as drug development.

Through the use of iPS cell technologies developed by Prof. Shinya Yamanaka of Kyoto University in 2006, research has made great advances even in diseases that were difficult to be investigated by conventional methods. In 2012, the Keio University School of Medicine became the first research facility in Japan to create iPS cells from patients with familial Parkinson's disease, and was successful in replicating the disease mechanism. Currently, research into neurological diseases has become very active throughout the world, and the understanding of diseases and development of new treatments is highly anticipated.

In April 2013, the Keio University School of Medicine and Eisai initiated the “Innovative Drug Discovery Project for Refractory Neurological Diseases Using iPS Cell Technologies,” and since then this drug discovery project has been progressing as an industry-academia collaboration, making full use of the Keio University School of Medicine's iPS cell and related technologies as well as Eisai's drug discovery techniques. Through this research, dopaminergic neurons which are thought to be damaged in Parkinson's disease patients were created efficiently and easily using iPS cells derived from Parkinson's disease patients, and an experimental system for conducting screening for drug discovery was established. In this research, Keio University School of Medicine's iPS cell and related technologies were used to efficiently generate Parkinson's disease patients, and an experimental system for conducting screening with an existing drug library, and suggested a broad range of potential for both the development of treatments and clarification of disease pathology through this research.

In this research, neural progenitor cells induced from iPS cells established from two familial Parkinson's disease (PARK2) patients were used to efficiently generate dopaminergic neurons. In patient-derived neurons, reduced neurite length as well as elevated oxidative stress and apoptosis were observed compared to neurons derived from healthy controls. Furthermore, it was revealed that these disease-relevant phenotypes were also observed in dopaminergic neurons derived from isogenic PARK2 null iPS cells obtained by genome editing.

In addition, since patient-derived dopaminergic neurons showed high susceptibility to rotenone, a mitochondrial respiratory chain complex I inhibitor, an existing drug library was screened with this method, it is hoped that this will lead to application in the development of a fundamental treatment for Parkinson's disease. Going forward, this research will continue, the knowledge gained will be further developed and experimental systems closely reflecting the brain environment in vivo, such as co-cultured neurons with glial cells, will be utilized in an effort to verify the validity of targets for Parkinson's disease.

Further detailed analysis conducted by the research group revealed higher expression of T-type calcium channels in dopaminergic neurons derived from Parkinson's disease patients. It was also found that apoptosis of dopaminergic neurons derived from Parkinson's disease patients could be reduced by inhibiting calcium influx via T-type calcium channels.

From these results, using iPS cells derived from patients enabled the establishment of in-vitro disease models that reflect human biology, and by further combining with existing drug library, suggested efficacy for drug screening. By promoting the understanding of disease pathology through this method, it is hoped that this will lead to application in the development of a fundamental treatment for Parkinson's disease. Going forward, this research will continue, the knowledge gained will be further developed and experimental systems closely reflecting the brain environment in vivo, such as co-cultured neurons with glial cells, will be utilized in an effort to verify the validity of targets for Parkinson's disease.
A year in review and a year's preview

BY BRUCE POORMAN, PUBLISHER & LAURENCE DOYLE, ASSOCIATE PUBLISHER

O
nce again, the end of the year is upon us. Well, not literally, unless you happen to be opening this issue on Dec. 31 to read this, but with our last issue of 2018 now in your hands (or on your screen), we wanted to thank you for your continued readership and welcome you in advance to another year of pharma and biotech news from discovery to development to trials—and sometimes beyond.

Our coverage of therapeutic areas includes coverage of the under-served disease NASH (see “A look in the markets on page 3), in which we are seeing a boom in liver disease therapeutics, especially this year, from CRISPR gene editing to neuro-epigenetics, drug delivery, stem cells, molecular diagnostics, and a plethora of news stories spanning the entire range of therapeutics and diagnostics.

Thanks as always for being on this ride with us, and we can’t wait to see you in 2019 so we can all break our new year’s resolutions while staying up to date with pharma and biotech news.

Laurence Doyle and Bruce Poorman

For more information, visit www.DDN-News.com

Peter T. Kissinger

HEART TRANSPARENCY VS. OPAQUE

THE OPINIONS EXPRESSED IN GUEST COMMENTARIES DO NOT NECESSARILY REPRESENT THOSE OF DDN-NEWS AND/OR ITS OWNERS, EDITORS OR OTHER STAFF.

For the under-served disease NASH (see “A look in the markets on page 3), in which we are seeing a boom in liver disease therapeutics, especially this year, from CRISPR gene editing to neuro-epigenetics, drug delivery, stem cells, molecular diagnostics, and a plethora of news stories spanning the entire range of therapeutics and diagnostics. Thanks as always for being on this ride with us, and we can’t wait to see you in 2019 so we can all break our new year’s resolutions while staying up to date with pharma and biotech news.

Laurence Doyle and Bruce Poorman

For more information, visit www.DDN-News.com

Peter T. Kissinger
COMMENTARY: A more reproducible approach to creating functional Th17 cells

BY KEVIN BOBOFCHAK, GLOBAL PRODUCT MANAGER, LONZA

C OVERLY LINED WITH various inflammatory and autoimmune disorders, Th17 cells are an attractive therapeutic target, and are at present the focus of many cancer immunotherapy research projects. However, current methods of generating Th17 cells are time-consuming, costly and often cause significant intra- and inter-laboratory variability, calling into question the relevance of the results.

Developing an alternative approach for the creation of functional Th17 cells that improves experimental reproducibility by simplifying the differentiation process has long been a goal of researchers in the field. A novel method of bead-based activation from cryopreserved CD4+ T cells has been developed that offers the potential to generate physiologically relevant Th17 cell populations suitable for wide range of downstream assays.

In this article, we consider the importance of Th17 cell biology and look at how the use of specialized methods to confirm cellular identity provides a level of validation that has not previously been available.

Th17 cells: An attractive therapeutic target

Th17 cells are one of a number of different subsets of T helper (Th) cells. Characterized by production of the pro-inflammatory cytokine IL-17, they are derived from CD4+ T cells. However, Th17 cells have recently been developed that enhances experimental reproducibility while shortening timelines, cutting costs and eliminating the risks of working with human whole blood.1

In this protocol, highly pure cryopreserved CD4+ T cells are simply thawed and mixed with specialized beads coated with antibodies against CD2, CD3 and CD28 molecules. These mimic antigen-presenting cells (APCs), to which the CD4+ T cells are attracted, and also activate resting T cells. Following the addition of a defined mixture of cytokines and antibodies, and subsequent incubation, the CD4+ T cells differentiate into the Th17 cell lineage.

This novel method of Th17 cell creation is far less prone to error than traditional methods because the entire process is greatly simplified. Rather than having to isolate CD4+ T cells from human whole blood, which can result in preparations that may be contaminated with many other cell types, researchers can instead access a highly pure CD4+ T cell population. Bead-based activation of these cells represents a more standardized method of differentiation.

An additional advantage of using cryopreserved CD4+ T cells is that each vial contains a defined number of viable cells. This obviates the need to adjust experimental conditions to align with cell populations. Furthermore, with CD4+ T cells available from multiple donors to afford a wide research demographic, and with alternative cell types available from the same donor, a greater breadth of data can be achieved.

A fully validated process

Validation of Th17 cell creation has traditionally relied on flow cytometric analysis; however, this can be extremely challenging since very few surface molecules are expressed exclusively by Th17 cells and there is a lack of specific antibodies that target these molecules. As a result, cells can often be mistaken.

Bead-based activation provides much greater confidence in Th17 cell identification since the process has been validated via multiple and independent methods. During phenotypic characterization clumping around the beads and increased proliferation are positive indicators of differentiation. Quantitation of IL-17 secretion into the growth medium using a bead-based proximity assay provides further confirmation of Th17 cell identity. This is supported by the use of RNA fluorescence in situ hybridization (RNA FISH) to detect IL-17 gene expression at the mRNA level. In combination, these techniques provide a more definitive method of confirming Th17 cell creation.

Streamlining drug discovery

The use of high-quality, commercially available CD4+ T cells in combination with specialized reagents to promote Th17 cell differentiation offers many advantages for drug discovery. Most notably, the quality of data that is produced using Th17 cells is greatly enhanced relative to traditional approaches. Because these cells are more physiologically relevant than preparations that may be contaminated with other cell types, this translates into more effective design-making that can streamline the drug discovery process. Additionally, this approach is significantly faster, as timelines are shortened by elimination of time-consuming CD4+ T cell isolation steps. This also contributes to safer working practices, while simplification of the differentiation process may also expedite drug development. Moreover, Th17 cells can also provide substantial cost savings through decreased manual processing steps, a reduced need to perform repeat experiments, and elimination of the expense associated with human whole blood work.

Similar combinations of cryopreserved cells, simplified differentiation methods and standardized protocols hold enormous potential for the generation of other specialized immune cells to advance research and drug discovery. Bead-based activation represents a major advance in immune cell creation and offers huge possibilities for the future.

REFERENCES


KISSINGER

EDITORIAL

KISSINGER CONCLUDED FROM PAGE 10 are not clearly revealed. Recently, the United Kingdom’s House of Commons and Technology Committee issued a discouraging report on the topic. They are not alone.

Healthcare pricing also appears to be all about opacity. The supply chain complexities work against patients. Patients see nothing equivalent to a menu of priced options as we do in a restaurant or on the window of a new vehicle. Until this is fixed, opacity will keep winning and healthcare will not benefit from the new productivity that informatics has brought to other sectors. The recent U.S. Health and Human Services proposal to refer to prices in public drug advertisements is as interesting as was the insistence on reference to side effects.

Are the “peers” an elite to be protected, or exposed? The whistles are blowing for transparency. Top people at top institutions have failed us, very recently at Sloan Kettering and Duke.

On the other hand, government is not an effective way to make it happen. Ratting off side effects with no reference to their probabilities is silly, as would be a comparison of prices in a dozen countries. Prices are a variable. Witness holiday sales. I would prefer a blanket statement saying, “all drugs have adverse results in some people, read the product insert before swallowing and ask about pricing.”

It’s tough in this sector because there is not a standard payment system used to produce consistent people as there is with a capsule, a medical device or a car. Nevertheless, we can do better with transparency. Educating the public on the opaque areas of the drug business costs lives and we can afford it.

Are the “peers” an elite to be protected, or exposed? The whistles are blowing for transparency. Top people at top institutions have failed us, very recently at Sloan Kettering and Duke.

On the other hand, government is not an effective way to make it happen. Ratting off side effects with no reference to their probabilities is silly, as would be a comparison of prices in a dozen countries. Prices are a variable. Witness holiday sales. I would prefer a blanket statement saying, “all drugs have adverse results in some people, read the product insert before swallowing and ask about pricing.”

It’s tough in this sector because there is not a standard payment system used to produce consistent people as there is with a capsule, a medical device or a car. Nevertheless, we can do better with transparency. Educating the public on the opaque areas of the drug business costs lives and we can afford it.

Peter T. Kissingер (who can be reached at kissing@ddn-news.com) is professor of chemistry at Purdue University, chairman emeritus of BASi (www.basi.com), and Kettering and Duke.

On the other hand, government is not an effective way to make it happen. Ratting off side effects with no reference to their probabilities is silly, as would be a comparison of prices in a dozen countries. Prices are a variable. Witness holiday sales. I would prefer a blanket statement saying, “all drugs have adverse results in some people, read the product insert before swallowing and ask about pricing.”

It’s tough in this sector because there is not a standard payment system used to produce consistent people as there is with a capsule, a medical device or a car. Nevertheless, we can do better with transparency. Educating the public on the opaque areas of the drug business costs lives and we can afford it.
**RESEARCH & DEVELOPMENT**

**Fast, open and free analysis with BioJupies**

Mount Sinai researchers develop tool that analyzes biomedical data within minutes

BY MEL J. YEATES

NEW YORK—Researchers at the Icahn School of Medicine at Mount Sinai have developed a tool that speeds up the analysis and publication of biomedical data from months or years to minutes, potentially transforming the way researchers can communicate the results of their studies.

Until now, the primary method available to share biomedical research data has been through print publication in scientific journals. This new tool, BioJupies, relies on cloud technology to analyze and visualize large amounts of data, such as that acquired by genome sequencing. The results were described in an article in the November issue of Cell Systems.

RNA sequencing is the most common experimental method used to profile cells in biomedical research. In recent years, sequencing technology has revolutionized the way scientists examine genetic data, and this advancement plays a crucial role in drug discovery and development. Traditionally, RNA sequencing requires extensive computer programming skills and access to local high-performance computing facilities, slowing down the speed at which biomedical data can be analyzed, shared, and published.

“BioJupies is an online software system that guides a user through a step-by-step process. The first step asks the user to upload their raw RNA-sequencing data to our server. Once the data is uploaded, we align the raw reads to the reference genome using a very efficient and low-cost pipeline that is running on the Amazon cloud. This step is currently a bottleneck for many researchers because of cost, access to high-performance computing and required knowledge of computer programming,” says Dr. Avi Ma’ayan, director of the Mount Sinai Center for Bioinformatics, a professor in the Department of Computer Science and director of the Mount Sinai Center for Bioinformatics.

Researchers at the Icahn School of Medicine at Mount Sinai say they have created a tool capable of reducing analysis and publication of biomedical data from months to minutes.

**Understanding Zika’s methods**

New lab technique helps reveal how Zika virus manipulates the immune system by stripping immune cells of their identity

BY KRISTEN SMITH

SAN DIEGO—Despite a global slowdown in Zika infections, researchers are still working to better understand the complicated mechanisms of the virus. Researchers at the University of California, San Diego (UC San Diego)—using a technique to label, or tag, infected and non-infected cells in a culture—have revealed the key mechanisms the Zika virus (ZIKV) uses to outsmart the immune system. Their findings, recently published in the journal Proceedings of the National Academy of Sciences, illuminate how Zika is able to stop macrophages from performing their key functions for immune cell recruitment and antiviral defense.

Zika has proven to be much more effective at penetrating the body’s natural barriers against infections than other viruses, primarily because of its effect on an immune cell type called a macrophage. Researchers knew that macrophages are a key part of the immune system that protects us from viral infections, but wanted to better understand how Zika successfully infects those cells that normally kill viruses. “How Zika virus (ZIKV) is able to infect different cell types and cause human disease/ pathology is not well understood,” according to Dr. Aaron Carlin, an associate physician in the Department of Medicine at Mount Sinai School of Medicine.

“Flaviviruses, like ZIKV, are known to infect macrophages. However, it is not clear how they do so, or how they manipulate the macrophage to their benefit,” says Dr. Carlin. “Using a combination of bioinformatic analysis and functional assays, we were able to show how macrophages are infected and how the virus manipulates the immune system against us.”

“ZIKV macrophages can be seen as vehicles for disseminating the virus throughout the body,” says Dr. Carlin. “Our findings show that ZIKV manipulates the immune system by stripping immune cells of their identity.”

“By removing their identity, ZIKV macrophages are able to use the body’s own defenses against itself,” says Dr. Carlin. “This is a groundbreaking discovery that will help us develop new treatments for Zika infection.”

**A challenge for Alzheimer’s innovation**

Business leader fuels global, multimillion-dollar Oskar Fischer Project

BY JEFFREY BOULEY

SAN ANTONIO—Alzheimer’s disease has vexed researchers and clinicians for years, leaving them with plenty of questions and clues but precious little in the way of answers or successful paths toward treatment. To help remedy that, U.S. businessman James Truchard has given a $5 million gift to the University of Texas at San Antonio (UTSA) College of Sciences to establish the Oskar Fischer Project—a move announced at the Society for the Challenge continued on page 13

**IN THIS SECTION**

Data analysis/Genomics

Fast, open and free analysis with BioJupies

Infectious disease

Arrowhead, Janssen ink new deals

Combination regimens vs. antibiotic resistance

Understanding Zika’s methods

Neurology

A challenge for Alzheimer’s innovation

Combination regimens vs. antibiotic resistance

Fast, open and free analysis with BioJupies

Arrowhead, Janssen ink new deals

Understanding Zika’s methods

A challenge for Alzheimer’s innovation
and found it to produce comparably marked kallisto with other aligners allowing for 300,000 publicly available datasets. BioJupies also produces data processing to less than one cent per sample. BioJupies paves the way for researchers with no computational background to perform RNA sequencing analysis without the need to collaborate with bioinformaticians, enabling more medical and scientific advancements to flourish in our data-rich world.

The ultimate purpose of the tool is to make it much easier for experimentalists to analyze and share their data. Ultimately, the notebooks generated by BioJupies are similar to a research publication but they also contain source code and interactive figures... So BioJupies, and tools like it, may change the way researchers publish their work,” adds Ma’ayan. “The approach can be expanded to handle other data types. We hope that the community will contribute analysis plug-ins so users will be able to have a greater selection of analysis tools to choose from. We also plan to have a place for people to publish their notebooks in an online journal so notebooks can be cited by other notebooks and other forms of publication.”

BioJupies is freely available as a web-based application at http://biojupies.cloud.

“Once the raw RNA-sequencing data are aligned, the user selects the visualization and analysis tools they would like to apply to the processed data,” Ma’ayan adds. “Once these tools are selected, BioJupies generates a Jupyter notebook analysis report from the data. The analysis report contains interactive figures, tables and text that describes the analysis. The online report also has the source code of the analysis so others can run the analysis or modify it and customize it. It is completely free and available to anyone. It is also an open-source project.”

“BioJupies enables the generation of Jupyter Notebooks from RNA-seq data in both raw and processed forms. In case of processed RNA-seq data, the user uploads numeric gene counts in a tabular format,” the authors wrote in the paper. “This can be an Excel spreadsheet or a comma-separated text file containing gene symbols as row names, samples as the column names, and gene counts as values. In addition, metadata that describes the samples can be uploaded in a separate Excel spreadsheet or a comma-separated text file. A detailed explanation of the format to upload the data, including links to download example datasets, is provided on the BioJupies website’s help section.

“In the case of raw RNA-seq data, the user is provided with a user interface that enables them to upload FASTQ files through an HTML form. The user is required to specify the organism, and whether the RNA-seq data were generated using single-end or paired-end sequencing. Once this information is collected, gene expression levels for each gene are quantified by launching parallel jobs in the cloud using the kallisto pseudocaligner (Bray et al., 2016). We have benchmarked kallisto with other aligners and found it to produce comparable count accuracy at a significant lower cost (Lachmann et al., 2018)...

Once the quantification step is complete, which may take up to 15 min, sample counts are merged to generate a gene count matrix. From that point on, the user follows the same steps to generate notebooks as with processed uploaded data (gene counts matrix), by adding sample metadata and selecting the analysis tools they wish to employ.”

Through BioJupies, users reportedly can upload and analyze their RNA sequencing data in a fraction of the time. The platform utilizes a cloud computing pipeline that reduces the cost of RNA sequencing data processing to less than one cent per sample. BioJupies also produces a complete, open-source, interactive report from the processed data, allowing for 300,000 publicly avail-
Scientists describe DNA recombination in Alzheimer’s disease brains, related to APP gene and HIV-linked enzyme

BY JEFFREY BOULEY
LA JOLLA, Calif. & ORLANDO—In a study published in Nature, researchers at the Sanford Burnham Prebys Medical Discovery Institute (SBP) report that they identified never-before-seen gene recombination in neurons that produces thousands of new gene variants within Alzheimer’s disease (AD) brains, revealing for the first time how the Alzheimer’s disease-linked gene known as APP is recombined by using the same type of enzyme found in HIV.

The scientists found that the gene recombination process required an enzyme called reverse transcriptase, the same type of enzyme HIV uses to infect cells. SBP stresses that there is no medical evidence that HIV or AIDS cause AD; however, existing FDA-approved antiretroviral therapies for HIV that block reverse transcriptase might, the institute says, “also be able to halt the recombination process and could be explored as a new treatment for Alzheimer’s disease. The scientists noted the relative absence of proven Alzheimer’s disease in aging HIV patients on antiretroviral medication, supporting this possibility.”

“Our findings provide a scientific rationale for immediate clinical evaluation of HIV antiretroviral therapies in people with Alzheimer’s disease,” said Dr. Jerold Chun, senior author of the paper and the senior vice president of neuroscience drug discovery at SBP. “Such studies may also be valuable for high-risk populations, such as people with rare genetic forms of Alzheimer’s disease.”

Added first author Dr. Ming-Hsiang Lee, a research associate in the Chun laboratory, “Reverse transcriptase is an error-prone enzyme, meaning it makes lots of mistakes. This helps explain why copies of the APP gene are not accurate in Alzheimer’s disease and how reverse transcription and reinsertion of the variants back into the original genome, producing permanent DNA sequence changes within the cell’s DNA blueprint.”

“We used new approaches to study the APP gene, which gives rise to amyloid plaques, a pathological hallmark of the disease,” explained Chun. “Gene recombination was discovered as an indirect link between Alzheimer’s and HIV. Our findings provide a scientific rationale for testing existing FDA-approved antiretroviral drugs for HIV to evaluate effectiveness in AD patients. Studies could begin right away, because these drugs have already undergone extensive safety testing and have been used safely for years to treat HIV.”

One hundred percent of the AD brain samples contained an over-abundance of distinct APP gene variants, compared to samples from normal brains. Among these Alzheimer’s-enriched variations, the scientists identified 11 single-nucleotide changes identical to known mutations in familial AD, a very rare inherited form of the disorder. Although found in a mosaic pattern, the identical APP variants were observed in the most common form of Alzheimer’s disease, further linking gene recombination in neurons to disease.

“These findings may fundamentally change how we understand the brain and Alzheimer’s disease,” noted Chun. “If we imagine DNA as a language that each cell uses to ‘speak,’ we found that in neurons, just a single word may produce many thousands of new, previously unrecognized words. This is a bit like a secret code embedded within our normal language that is decoded by gene recombination. The secret code is being used in healthy brains but also appears to be disrupted in Alzheimer’s disease.”

And if the research findings are applicable to actual curative results in AD patients, the benefits could be reaped very soon. “There is currently no way to prevent, treat or cure AD. The healthcare and societal impacts of AD are increasing as the U.S. population ages. An effective treatment is urgently needed. This study identifies an underlying cause of the disease, and points to a near-term treatment for AD,” Chun said. “On average, it takes 10 years for a drug to receive FDA approval. This study provides scientific rationale for testing existing FDA-approved antiretroviral drugs for HIV to evaluate effectiveness in AD patients. Studies could begin right away, because these drugs have already undergone extensive safety testing and have been used safely for years to treat HIV.”

The findings could also go a long way toward explaining why clinical trials in experimental AD drugs have been such a disappointment so far. As SBP notes, the amyloid hypothesis—the theory that accumulation of a protein called beta-amyloid in the brain causes AD—has driven most of the Alzheimer’s research to date. However, treatments that target beta-amyloid have, as SBP put it, “notoriously failed in clinical trials.”

“The failures of AD clinical trials may reflect that there are many more forms of toxic variants of APP (amyloid precursor protein) than previously thought,” Chun remarked. “APP is a gene known to be associated with AD—and these APP variants were most likely missed by drugs targeting the single form of APP.”

“One hundred percent of the AD brain samples contained an over-abundance of distinct APP gene variants, compared to samples from normal brains. Among these Alzheimer’s-enriched variations, the scientists identified 11 single-nucleotide changes identical to known mutations in familial AD, a very rare inherited form of the disorder. Although found in a mosaic pattern, the identical APP variants were observed in the most common form of Alzheimer’s disease, further linking gene recombination in neurons to disease.”

“Gene recombination was discovered as an indirect link between Alzheimer’s and HIV. Our findings provide a scientific rationale for testing existing FDA-approved antiretroviral drugs for HIV to evaluate effectiveness in AD patients. Studies could begin right away, because these drugs have already undergone extensive safety testing and have been used safely for years to treat HIV.”

Chun says that his team’s discovery is a step forward, but “there is so much that we still don’t know;” he acknowledges. “We hope to evaluate gene recombination in more brains, in different parts of the brain and involving other recombined genes—in Alzheimer’s disease as well as other neurodegenerative and neurological diseases—and use this knowledge to design effective therapies targeting gene recombination.”
CHALLENGE
CONTINUED FROM PAGE 12
Neuroscience’s annual meeting in early November.
Truchard, the retired president and CEO of tech company National Instruments, presented the idea of the Oskar Fischer Project with an eye toward engaging the brightest minds in the world to work on expanding the understanding of the and the explanations for Alzheimer’s disease. The challenge will award up to $14 million in Oskar Fischer Prizes, including a grand prize of $2 million, two second place prizes of $500,000 each and four third place prizes of $250,000 each. Collectively, the monetary awards are the world’s largest prizes of their kind, according to UTSA.

The name of the project comes from Truchard’s personal research that introduced him to the work of the late Oskar Fischer, a Jewish pioneer in neuroscience who studied dementia at the same time as Alois Alzheimer did. In 1900, Fischer began working at Charles University’s German University, based in Prague, and his research led to the identification of senile plaques—which were then referred to as neuritic plaques—the lesions which continue to be considered a hallmark of Alzheimer’s disease.

Fischer hypothesized that the plaques were associated with presbyophrenia, then characterized as a form of senile dementia marked by memory loss, memory distortions and disorientation. He published on 12 patients with plaques and tangles, protein strands that appear during Alzheimer’s disease, in 1907, the same year that Alzheimer published—on one patient with early-onset Alzheimer’s.

Fischer remained at the German University until he was removed in 1939. Two years later, he was sent to Theresienstadt in Terezín, a waystation for Auschwitz and Theresienstadt. He died in 1942, unable to survive the harsh conditions of the concentration camp.

“Academy has passed since Oskar Fischer’s seminal work, and tens of billions have been spent around the world on research and potential cures. Over 130,000 research papers have been published and yet no definitive explanation and cure for Alzheimer’s has been found,” said Truchard. “We need to look at Alzheimer’s as a big complex puzzle with a missing piece. We need a brilliant individual who can take all of the pieces and consider what each offers, and then develop one explanation that fits because it pulls all of the pieces together and makes the puzzle whole.”

“The Oskar Fischer Project will take a new systems approach to the challenge that will engage scientists on the goal of innovation in the field of Alzheimer’s disease.”

UTSA, which positions itself as “a world leader in brain health research,” will incubate the two-year challenge. In the UTSA Brain Health Consortium, nearly 40 scientists are already engaged in research on brain mechanisms and therapeutics. The university’s researchers have expertise in neurodegenerative disease, brain circuits and electrical signaling, traumatic brain injury, regenerative medicine and stem cell therapies, medicinal chemistry and drug design, neuroinflammation and psychology.

“Through Jim Truchard’s support, the Oskar Fischer Project will accelerate our shared mission of unraveling the mysteries of neurodegeneration through engagement with the smartest thinkers around the world,” said UTSA President Taylor Eighmy.

For more information, visit www.DDN-News.com

DECEMBER 2018 || DDNEWS 15
Negating nicotine

**Scripps scientists test enzyme to reduce dependence**

BY ILENE SCHNEIDER

LA JOLLA, Calif.—“Tobacco use disorder is responsible for over 400,000 deaths annually in the United States. It is critical to develop novel approaches to reduce the psychoactive effects of nicotine, decrease craving, and prevent relapse,” wrote scientists at Scripps Research, who have successfully tested a potential new smoking-cessation treatment in rodents in a study (“An enzymatic approach reverses nicotine dependence, decreases compulsive-like intake, and prevents relapse”) published online in Science Advances in October.

While tobacco use disorder is a leading cause of disease and preventable death worldwide, currently available medications based on pharmacodynamics have low efficacy, the Scripps scientists said, adding, “Novel pharmacokinetic approaches to prevent nicotine from reaching the brain have been tested using vaccines, but these efforts have failed because antibody affinity and concentration are not sufficient to completely prevent nicotine from reaching the brain.”

With funding provided by the National Institute on Drug Abuse, the researchers gave nicotine-dependent rats an engineered enzyme—NicA2-J1, an engineered nicotine-degrading enzyme that was originally isolated from *Pseudomonas putida* strain S16—to break down nicotine in the bloodstream before it can reach the brain. The treatment quickly reduced the animals’ motivation to take nicotine, reversed their signs of nicotine dependence on a stabilized trimeric enzyme to reduce nicotine cravings, and decreased compulsive-like intake before it could reach the brain.

The authors note that the treatment option is currently being tested in patients in a phase-1 clinical trial. They added, “The screening of the NicA2-J1 enzyme to reduce nicotine dependence could provide a low-invasive and convenient smoking-cessation therapy.

**Heralding HERA-CD27L**

**Preclinical efficacy data of Apogenix compound published in *Frontiers in Oncology***

BY MEL J. YEATES

HEIDELBERG, Germany—In October, Apogenix announced that new data published in *Frontiers in Oncology* demonstrate the potent antitumor efficacy of Apogenix’s HERA-CD27L. In contrast to antibodies in development, HERA-CD27L is the first true CD27 receptor agonist with a well-defined mode of action that acts directly on immune cells, thereby enhancing their antitumor immunity.

“Many key immune stimulatory proteins belong to the tumor necrosis factor superfamily (TNFSF) and their cognate receptors, the TNF receptor superfamily (TNFRSF). These important target receptors include CD27, GITR, OX40, 4-1BB, CD40 and HVEM,” notes Dr. David Richards, head of immunology at Apogenix. “Although many companies have been trying (and failing) to stimulate these receptors for over a decade, the field is only recently beginning to accept that antibodies are not the correct tool to stimulate the TNFRSF. Due to the dependency on a stabilized trimeric receptor complex for signaling, it is clear that flexible bivalent antibodies are not able to act as TNFRSF agonists.”

“Recently, multiple companies have started to explore the HERA ligand-based drug design pioneered by Apogenix,” he continues. “This shift shows promise and suggests that we might finally bring a stimulatory immunotherapy drug to the market to join the checkpoint inhibitors. HERA-CD27L is a promising development candidate that has been generated using our HERA-ligand technology platform.”

HERA-CD27L was generated using the Apogenix single-chain TNFSF technology, which is designed in a way that resembles the natural TNFSF receptor-binding domain, the company says. HERA-CD27L has a double trivalent, or hexavalent, structure composed of two single-chain antibody domains.

**Preventing heart disease in cancer survivors**

**CDK2 protein said to play critical role in heart damage caused by doxorubicin, a common chemotherapy drug**

BY DDNEWS STAFF

SPokane, Wash.—One doesn’t usually think of cancer and cardiovascular disease at the same time, but there is reason to because of doxorubicin, a commonly used chemotherapy drug that can cause heart damage. But if researchers at Washington State University (WSU) have their way, we will be thinking of tumors and heart disease together even less, as they say that a protein called CDK2 is the culprit in doxorubicin-induced heart damage. Their findings were published recently in the *

**IN THIS SECTION**

Addiction/Dependence

Negating nicotine .......................................... 16

Liver disease

Innate looking for answers about NASH (INNOVATE from cover) .... 18

Oncology

Heralding HERA-CD27L ................................... 16

Apogenix shares immunotherapy program results at SITC .......... 16

KD033 shows promise in tumor models ........................ 16

Oncology/Cardiovascular

Preventing heart disease in cancer survivors ....................... 16
“Access to nicotine again,” the researchers said, “leaves them in deep dependence and keeps them from quitting even when they were given access to nicotine again.”

Just as relapsing when they were given access to nicotine, the animals regained access. The animals deepening their addiction, when access periods, compared with untreated controls.

NicA2-J1 continued to self-administer with the highest dose of nicotine and became dependent on it. Then they were given much reduced access to nicotine when available but showed very low blood levels of nicotine activity, there will be immediate withdrawal symptoms. According to George, “What’s unique about this enzyme is that it removes enough nicotine to reduce the level of dependence but leaves enough to keep the animals from going into severe withdrawal.”

The researchers also showed that NicA2-J1 could reduce this compulsive motivation for nicotine in the addicted rats. When each lever-press for nicotine also brought a 30 percent chance of receiving an electric shock to the feet, the NicA2-J1-treated rats—unlike untreated controls—quickly reduced their lever presses.

To determine susceptibility to relapse after abstinence, the researchers removed the rats from nicotine for 10 days, then gave them an injection of nicotine to reawaken their desire for the drug and restored access via the lever-presses. Untreated rats increased their lever presses by a large amount, but NicA2-J1 treated rats did it much less.

The Scripps Research team hopes to take NicA2-J1 into clinical trials in humans. They will attempt to optimize NicA2-J1’s properties as a drug. They also plan to test it in rats against varenicline (Chantix), a compound that blocks nicotine activity in the brain and is currently viewed as the most effective smoking-cessation drug.

The enzyme provides efficacy in a simple rat model of nicotine dependency. “This is a very exciting approach because it can reduce nicotine dependence without inducing cravings and other severe withdrawal symptoms, and it works in the bloodstream, not the brain, so its side effects should be minimal,” says principal investigator Dr. Olivier George, an associate professor at Scripps Research. “These results demonstrate the efficacy of enzymatic therapy in treating nicotine addiction in advanced animal models and provide a strong foundation for the development of biological therapies for smoking cessation in humans.”

The enzyme was developed in George’s laboratory, which better mimic human smoking-cessation drug. This is a very exciting approach because it can reduce nicotine dependence without inducing cravings and other severe withdrawal symptoms, and it works in the bloodstream, not the brain, so its side effects should be minimal,” says principal investigator Dr. Olivier George, an associate professor at Scripps Research. “These results demonstrate the efficacy of enzymatic therapy in treating nicotine addiction in advanced animal models and provide a strong foundation for the development of biological therapies for smoking cessation in humans.”

While most people are aware of the harm smoking can do, nicotine dependence keeps them smoking. About 60 percent of the people who try cigarettes end up as daily smokers, and about 75 percent of daily smokers relapse after quitting. While reversing nicotine dependence by preventing the nicotine in tobacco smoke from reaching the brain has been considered a promising strategy, previous efforts have not yielded drugs that reduce blood levels of nicotine enough to be effective.

NicA2-J1, a version of a natural enzyme produced by the bacterium Pseudomonas putida, was modified to optimize its potency, its staying time in the blood and other pharmacological properties by the laboratory of Dr. Kim Janda, the Ely R. Callaway, Jr., Professor of Chemistry at Scripps Research. Previous studies have shown that NicA2-J1 strongly reduces blood levels of nicotine in rodents and provides efficacy in a simple rat model of nicotine dependency.

The new study tested the enzyme in more sophisticated animal models, developed in George’s laboratory, which better mimic human smokers’ addiction to nicotine.

In one set of experiments, lab rats learned to self-administer nicotine and became dependent on it. Then they were given much reduced access to nicotine, leading them to experience withdrawal symptoms between access periods, and to increase their intake, thus deepening their addiction, when they regained access. The animals treated with the highest dose of NicA2-J1 continued to self-administer nicotine when available but showed very low blood levels of the molecule compared to controls.

Signs of nicotine withdrawal were correspondingly reduced during the no-access periods, compared with untreated controls.

“It’s as if they were smoking 20 cigarettes but receiving the nicotine dose of only one or two, so that made their withdrawal process much less severe,” explained study first author Dr. Marsida Kallupi, a postdoctoral research associate in the George Laboratory.

NicA2-J1 continued to self-administer nicotine when available but showed very low blood levels of nicotine activity, there will be immediate withdrawal symptoms. According to George, “What’s unique about this enzyme is that it removes enough nicotine to reduce the level of dependence but leaves enough to keep the animals from going into severe withdrawal.”

The researchers also showed that NicA2-J1 could reduce this compulsive motivation for nicotine in the addicted rats. When each lever-press for nicotine also brought a 30 percent chance of receiving an electric shock to the feet, the NicA2-J1-treated rats—unlike untreated controls—quickly reduced their lever presses.

To determine susceptibility to relapse after abstinence, the researchers removed the rats from nicotine for 10 days, then gave them an injection of nicotine to reawaken their desire for the drug and restored access via the lever-presses. Untreated rats increased their lever presses by a large amount, but NicA2-J1 treated rats did it much less.

The Scripps Research team hopes to take NicA2-J1 into clinical trials in humans. They will attempt to optimize NicA2-J1’s properties as a drug. They also plan to test it in rats against varenicline (Chantix), a compound that blocks nicotine activity in the brain and is currently viewed as the most effective smoking-cessation drug.
INNOVATE
CONTINUED FROM PAGE 1

affects an estimated 2 percent to 5 percent of the population. The underlying cause of NASH—which is a specific kind of non-alcoholic fatty liver disease (NAFLD)—is unclear aside from the fact alcohol use is not the culprit, but it most often occurs in persons who are middle-aged and overweight or obese. It has been shown that chronic liver diseases, including NAFLD/NASH, may cause perturbations in the epithelial lining of the gut and disrupt barrier integrity, causing a normal intestine to become more permeable. This “leaky gut” could cause passage of unrecognized toxins and antigenic components to “cross-talk” to the liver via the blood circulation causing inflammation and damage to hepatocytes. This gut-liver axis is an emerging area of research in chronic liver diseases, such as NAFLD/NASH. There are currently no FDA approved treatments for NAFLD/NASH.

The DIAMOND (Diet Induced Animal Model Of Non-alcoholic fatty Liver Disease) mice are a proprietary isogenic mouse strain licensed by Sanibal Biotechnology that develops NAPFLD, NASH, fibrosis and hepato-cellular carcinoma in response to a high fat high sugar Western Diet without poisons or other interventions. The mice become insulin-resistant, obese and dyslipidemic just like humans with metabolic syndrome, and disease progression parallels that of the human body right down to the histopathology.

Additionally, Innovate is looking for opportunities where larazotide may be used in conjunction with other drugs in late-stage clinical trials for NASH, which are already approved in other indications. Currently, Innovate is studying Novo Nordisk A/S’s Victoza (liraglutide) approved for type 2 diabetes and Intercept Pharmaceuticals Inc.’s Ocaliva (obeticholic acid) approved for primary biliary cholangitis in combination with larazotide in preclinical models with the goal of determining the optimal synergistic drug combination with different mechanisms of action.

We are very encouraged about how larazotide could synergistically work with drugs in late-stage clinical trials for NAFLD/NASH, which are already approved in other indications. We believe that larazotide’s more upstream mechanism of blocking the inflammatory cascade without impacting the liver directly may support its potential therapeutic effect in NAFLD/NASH,” says Dr. Christopher Prior, CEO of Innovate Biopharmaceuticals.

Larazotide works to renovitalize the dysfunctional intestinal barrier by decreasing intestinal permeability and reducing antigen trafficking, such as gliadin fragments in celiac disease, and bacterial toxins and immunogenic antigens in NASH. In several diseases—including celiac disease, NASH, Crohn’s disease, ulcerative colitis and irritable bowel syndrome—the intestinal barrier is dysfunctional with increased permeability. In celiac disease specifically, larazotide is the only drug that has successfully met its primary end point with statistical significance in a Phase 2b efficacy clinical trial of 342 patients. Innovate completed the End of Phase 2 Meeting with the FDA in 2017 and is preparing to begin Phase 3 registration clinical trials for celiac disease, targeted to commence in the first half of 2019. Nearly 600 subjects have been exposed to larazotide in clinical trials, and a safety profile comparable to placebo has been demonstrated, earning the drug Fast Track designation from the FDA for celiac disease.

Added Dr. Arun Sanyal, professor and chair of the Division of Gastroenterology, Hepatology and Nutrition at the Virginia Commonwealth University (VCU) School of Medicine: “Increased intestinal permeability has been linked to many aspects of metabolic syndrome, including type 2 diabetes and non-alcoholic fatty liver disease. The demonstration of reduced gut permeability with larazotide in the setting of diet-induced obesity opens up the possibility of modulating the outcomes of metabolic syndrome, including NASH, via this mechanism and warrants further development for these indications.”

Moving forward, Innovate plans to submit the complete NASH preclinical results for publication and to begin the Phase 2 trial in 2019. The company also intends to launch a clinical program in NASH with a Phase 2 trial in 2019. **

**EDITCONNECT: E121810

HERA
CONTINUED FROM PAGE 16

chain receptor-binding-domain modules linked together with an IgG1-Fc domain, which has been selected for its potent Fc receptor binding, and according to Richards: “This double trivalent, or hexavalent, structure has been shown to cluster a sufficient number of TNFRSF molecules in the correctly stabilized conformation to produce biological activity.” He adds that HERA-CD27L is a true TNFRSF agonist that provides a co-stimulatory signal in combination with a T cell receptor (TCR)-specific signal—together with the TCR signal, HERA-CD27L acts to boost specific T cell activation, proliferation and differentiation.

The strong antitumor efficacy of HERA-CD27L was demonstrated in two different tumor models—MC38-CEA and CT26-wt—as noted by the Frontiers in Oncology paper. Herbert, the clinic lead and group member in both doxorubicin and rosuvastatin—one immunosuppressive substance that selectively inhibits CD27—found that heart function in those mice was preserved. The same findings were also confirmed in rat heart cells. The study shows early promise that CDK inhibitor drugs could be used to stave off heart toxicity in patients being treated with doxorubicin.

CDK inhibitors are a newer class of anticancer drugs. Only three such drugs—palbociclib, ribociclib and abemaciclib—are currently FDA approved for the treatment of different types of breast cancers, while another dozen or so are being tested in clinical trials. “Our findings suggest that combining doxorubicin with a CDK inhibitor could be a viable strategy for protecting patients’ hearts while they are being treated for cancer,” Cheng said. “It could provide a much stronger anticancer effect with less toxicity to the heart.”

“Finally, antibodies have a functional Fc-receptor binding domain, while the IgG1 scaffold domain in HERA-CD27L has been mutated to prevent Fc-receptor binding. Fc receptor binding leads to degradation of the antibody and other immune-related adverse events seen with antibody-based therapies.”

The combination of HERA-CD27L with an anti-PD-1 anti-body revealed additive antitumor effects, highlighting the importance of both T cell co-stimulation and checkpoint inhibition in anti-tumor immunity.

“HERA-CD27L treatment stimulates T cell responses. Therefore, combination with checkpoint inhibitors and strategies that provide additional antigen-specific T cell populations (such as radiation therapy, chemotherapy, vaccination or CAR T cells) would make sense. In fact, we show in the manuscript an additive benefit of using HERA-CD27L together with PD-1 inhibition in a preclinical tumor model,” Rich-ards adds.

“Strategies to enhance the anti-tumor immune response have tremendous potential and are considered the future of cancer therapy,” adds Harald Frick, chief medical officer of Apogenix. “Apogenix has develop- ed the proprietary HERA-ligand enhanced antibody-based strategy or potent tumor necrosis factor superfamily (TNFRSF) receptor agonists that play a crucial role in the regulation of the immune response. These agonists overcomethe significant limitations of antibody-based approaches by inducing optimal assembly of the TNFRSF receptors.”

“We have recently completed the generation of a research cell bank for our lead candidate. We are now ready for GMP process for development, “ mentions Richards. “The development of a robust CMC process together with the respective preclinical IND-enabling studies will be the next essential development steps towards clinical trials.”

“CD27 is an important target due to its unique role in both initiating as well as maintaining T cell responses,” Frick added. “We are in the process of evaluating the antitumor efficacy for additional HERA-ligands in a variety of pre-clinical studies and look forward to advancing them to the next stage.”

**EDITCONNECT: E121813

**"We are excited about looking at how larazotide could synergistically work with drugs in late-stage clinical trials for NASH..." We believe that larazotide’s more upstream mechanism of blocking the inflammatory cascade without impacting the liver directly may support its potential therapeutic effect in NAFLD/NASH,” says Dr. Christopher Prior of Innovate Biopharmaceuticals.

**"We are excited about looking at how larazotide could synergistically work with drugs in late-stage clinical trials for NASH..." We believe that larazotide’s more upstream mechanism of blocking the inflammatory cascade without impacting the liver directly may support its potential therapeutic effect in NAFLD/NASH,” says Dr. Christopher Prior of Innovate Biopharmaceuticals.
A manufacturing organization, announced recently manufacturing of AAV for dengue, yellow fever, Zika and chikungunya. The mosquito genome could lead to new avenues for Aedes aegypti. Don’t shoot the messenger—

CAMBRIDGE, U.K.—Elpis Biomed Ltd., a start-up of the year honor of industry experts: Barbara Fleck of AstraZeneca/MedImmune, and the innovative companies such as life-science start-up companies. "We have assembled a team of experts, designed to simplify fed batch processes for a variety of final formulations with different pharmaceutical ingredients (APIs) and stable, pharmaceutical processes, designed to simplify fed batch processes and trial optimization includes using Medidata Edge to help site feasibility and selection on behalf of PPD’s commitment to innovation for advancing and accelerating the drug development process. “It is exciting for PPD and its employees to be recognized by Medidata for its commitment to innovation in accelerating the drug development process,” said Niklas Morton, senior vice president of site and patient access for PPD, who accepted the award on the company’s behalf. “Our collabora-

A more complete version of the Aedes aegypti mosquito genome could lead to new avenues for blocking the spread of insect-borne diseases such as dengue, yellow fever, Zika and chikungunya.

The Cambridge Independent Science Awards & Honors featured highlights from the 2018 Cambridge Independent Science Awards & Technology Awards. “Elpis is set to have a transforma-
tive impact in the fields of biomedical research, drug discovery and cell therapy,” said Dr. Mark Kotter, scientific founder of Elpis BioMed. “We have assembled a world-class team to fulfill our mission to ‘make cells easy.’ I am honored that our efforts have been recognized by such an outstanding panel of technology experts, and that Elpis has been chosen as Start-Up of the Year from a field of truly excellent start-up companies.” Elpis was chosen from a short list of innovative companies such as life-science startups Fluidic Analytics and Evenetics, as well as diagnostic firms PredictImmune and Kalium Diagnostics. The Cambridge Independent Science and Technology Awards are sponsored by local technology weightheys such as AstraZeneca/ MedImmune, and the awards this year were judged by a panel of industry experts: Barbara Fleck of Appleyard Lees; Paul Brackley, editor of the Cambridge Independent; Kristen Riley of Grant Thornton; Charles Cotton, entrepreneur and author of The Cambridge Phenomenon; Dr. Sabine Jaccard of AstraZeneca; and Niam Smith, from Woodfin Flores Solicitors. The judges were to be impressed by the unique quality of Elpis’s technology, which they believe has huge implications for biotechnology research.

Last years’ recipient of the award, STORM Therapeutics, has since gone on to raise €4 million of funding from Taiko Ventures, and appointed Nobel Prize Winner Prof. Thomas Cech as scientific advisor. According to Brackley, the judges had a challenging time because of the “phenome-
nal” standard and range of entries, saying: “It was an extremely high-quality field—a real showcase of the tremendous talent in this region.”

MilliporeSigma recognized for innovative products

BURLINGTON, Mass.—MilliporeSigma recently won two CPhI Pharma Awards for innovative products for the pharmaceutical industry. The awards were announced at CPhI’s award gala in Spain. CPhI (Convention on Pharmaceutical Ingredients) Pharma is a global organization that connects people within the pharmaceutical industry and celebrates thinkers, creators and companies breaking new ground.

"At MilliporeSigma, we provide innovations that help our customers advance science and accelerate access to better health for people everywhere," said Andrew Bulpin, head of process solutions at MilliporeSigma. "We are pleased that CPhI has recognized our commitment to drive the industry forward and empower researchers and scientists with products that improve drug development quality and efficiency.”

The company received the following awards:

• Partex MMX Excipient won for “Excellence in Excipients.” Partex MMX excipient is a new polyvinyl alcohol excipient for the formulation of stable amorphous solid dispersions by hot melt extrusion, providing enhanced solubility of active pharmaceutical ingredients (APIs) and stable, high drug loads. The new excipient is applicable for a variety of final formulations with different release kinetics and offers the formulator flexibility in designing a drug product that fits the respective API and desired therapeutic effect.

• MilliporeSigma’s modified amino acids won for “Excellence in Bioprocessing and Manufacturing.” The modified amino acids phospho-tyrosine diso-
dium salt and sulfo-cysteine sodium salt are compo-
ents for biomacronucleating and monoclonal antibody processes, designed to simplify fed batch processes in applying a single-feed strategy.

CPhI Pharma is a global organization that connects people within the pharmaceutical sector and creates opportunities for pharma companies to develop new business, meet customers, launch new products, promote brands and expand into new markets.

PPD receives award for clinical trial innovation

WILMINGTON, N.C.—Pharmaceutical Product Development LLC (PPD) has been honored by Medidata with its Medidata Accelerator Award, recognizing PPD’s commitment to innovation for advancing and accelerating the drug development process.

"It is exciting for PPD and its employees to be recognized by Medidata for its commitment to innovation in accelerating the drug development process,” said Niklas Morton, senior vice president of site and patient access for PPD, who accepted the award on the company’s behalf. “Our collabora-

Don’t shoot the messenger—
target their genome

A more complete version of the Aedes aegypti mosquito genome could lead to new avenues for blocking the spread of insect-borne diseases such as dengue, yellow fever, Zika and chikungunya.

The Cambridge Independent Science Awards & Honors featured highlights from the 2018 Cambridge Independent Science Awards & Technology Awards. “Elpis is set to have a transforma-
tive impact in the fields of biomedical research, drug discovery and cell therapy,” said Dr. Mark Kotter, scientific founder of Elpis BioMed. “We have assembled a world-class team to fulfill our mission to ‘make cells easy.’ I am honored that our efforts have been recognized by such an outstanding panel of technology experts, and that Elpis has been chosen as Start-Up of the Year from a field of truly excellent start-up companies.” Elpis was chosen from a short list of innovative companies such as life-science startups Fluidic Analytics and Evenetics, as well as diagnostic firms PredictImmune and Kalium Diagnostics. The Cambridge Independent Science and Technology Awards are sponsored by local technology weightheys such as AstraZeneca/ MedImmune, and the awards this year were judged by a panel of industry experts: Barbara Fleck of Appleyard Lees; Paul Brackley, editor of the Cambridge Independent; Kristen Riley of Grant Thornton; Charles Cotton, entrepreneur and author of The Cambridge Phenomenon; Dr. Sabine Jaccard of AstraZeneca; and Niam Smith, from Woodfin Flores Solicitors. The judges were to be impressed by the unique quality of Elpis’s technology, which they believe has huge implications for biotechnology research.

Last years’ recipient of the award, STORM Therapeutics, has since gone on to raise €4 million of funding from Taiko Ventures, and appointed Nobel Prize Winner Prof. Thomas Cech as scientific advisor. According to Brackley, the judges had a challenging time because of the “phe-

A more complete version of the Aedes aegypti mosquito genome could lead to new avenues for blocking the spread of insect-borne diseases such as dengue, yellow fever, Zika and chikungunya.

The Cambridge Independent Science Awards & Honors featured highlights from the 2018 Cambridge Independent Science Awards & Technology Awards. “Elpis is set to have a transforma-
tive impact in the fields of biomedical research, drug discovery and cell therapy,” said Dr. Mark Kotter, scientific founder of Elpis BioMed. “We have assembled a world-class team to fulfill our mission to ‘make cells easy.’ I am honored that our efforts have been recognized by such an outstanding panel of technology experts, and that Elpis has been chosen as Start-Up of the Year from a field of truly excellent start-up companies.” Elpis was chosen from a short list of innovative companies such as life-science startups Fluidic Analytics and Evenetics, as well as diagnostic firms PredictImmune and Kalium Diagnostics. The Cambridge Independent Science and Technology Awards are sponsored by local technology weightheys such as AstraZeneca/ MedImmune, and the awards this year were judged by a panel of industry experts: Barbara Fleck of Appleyard Lees; Paul Brackley, editor of the Cambridge Independent; Kristen Riley of Grant Thornton; Charles Cotton, entrepreneur and author of The Cambridge Phenomenon; Dr. Sabine Jaccard of AstraZeneca; and Niam Smith, from Woodfin Flores Solicitors. The judges were to be impressed by the unique quality of Elpis’s technology, which they believe has huge implications for biotechnology research.

Last years’ recipient of the award, STORM Therapeutics, has since gone on to raise €4 million of funding from Taiko Ventures, and appointed Nobel Prize Winner Prof. Thomas Cech as scientific advisor. According to Brackley, the judges had a challenging time because of the “phe-

A more complete version of the Aedes aegypti mosquito genome could lead to new avenues for blocking the spread of insect-borne diseases such as dengue, yellow fever, Zika and chikungunya.

The Cambridge Independent Science Awards & Honors featured highlights from the 2018 Cambridge Independent Science Awards & Technology Awards. “Elpis is set to have a transforma-
tive impact in the fields of biomedical research, drug discovery and cell therapy,” said Dr. Mark Kotter, scientific founder of Elpis BioMed. “We have assembled a world-class team to fulfill our mission to ‘make cells easy.’ I am honored that our efforts have been recognized by such an outstanding panel of technology experts, and that Elpis has been chosen as Start-Up of the Year from a field of truly excellent start-up companies.” Elpis was chosen from a short list of innovative companies such as life-science startups Fluidic Analytics and Evenetics, as well as diagnostic firms PredictImmune and Kalium Diagnostics. The Cambridge Independent Science and Technology Awards are sponsored by local technology weightheys such as AstraZeneca/ MedImmune, and the awards this year were judged by a panel of industry experts: Barbara Fleck of Appleyard Lees; Paul Brackley, editor of the Cambridge Independent; Kristen Riley of Grant Thornton; Charles Cotton, entrepreneur and author of The Cambridge Phenomenon; Dr. Sabine Jaccard of AstraZeneca; and Niam Smith, from Woodfin Flores Solicitors. The judges were to be impressed by the unique quality of Elpis’s technology, which they believe has huge implications for biotechnology research.

Last years’ recipient of the award, STORM Therapeutics, has since gone on to raise €4 million of funding from Taiko Ventures, and appointed Nobel Prize Winner Prof. Thomas Cech as scientific advisor. According to Brackley, the judges had a challenging time because of the “phe-
Combating cancer with creativity

A collection of some of the newest approaches to targeting cancer cells

BY KELSEY KAUSTINEN

The more we learn about cancer, the easier it is to see why the disease continues to stymie drug developers. From hijacking the vascular system to feed tumors and camouflaging itself from immune checkpoints, to evolving to develop resistance to previously effective drugs, cancer has dozens of ways to evade treatment. But researchers are proving just as inventive in finding new ways to target the disease, not just by blocking off how it spreads, but also by researching how to get around each new shield cancer puts in place. This year has been a productive one in terms of discovering new ways to target cancer, and as 2018 winds to a close, we’ve selected some of the most recent—and most cutting-edge—ways that the industry has found to come at cancer sideways.

Bacteria and toxicity

Off-target effects are a stumbling block for any kind of drug, but for cancer, where drugs must be strong enough to kill off resilient cells that are designed to survive and spread, unintended toxicity is a particular issue. The industry has been working to address this issue by using more tightly targeted therapeutics or combination approaches that allow for lower (and less toxic) doses, but The Scripps Research Institute (TSRI) is looking back to the start, to the very origin of such drugs.

The question TSRI explored in recent work was the mechanism by which the compounds that are engineered into natural product-based drugs are kept safe from their own toxicity.

The answer they discovered is tied to a class of natural products known as enediyynes, which are yielded by bacteria referred to as actinomycetes, which are found in soil. Two cancer drugs based on enediyynes have been approved, but treatment resistance is a common problem for these compounds.

The lab of Dr. Ben Shen, professor, co-chair of the Scripps Research Department of Chemistry and senior author on this latest work, has been focused on the exploration of enediyynes. Two mechanisms by which bacteria can protect themselves from enediyynes have previously been discovered, and in a recent Cell Chemical Biology study, Shen and his lab shared news of a third, which hinges on three genes: tmnS1, tmnS2 and tmnS3. These genes encode proteins that enable bacteria to resist a subset of enediyynes known as tiancimycins, which are being explored as a base for new cancer drugs.

Those proteins bind to tiancimycins, isolating them from the rest of the organism, according to a TSRI press release. Shen and his team also identified the three tmnS genes in microorganisms present in the human microbiome.

Shen noted that this implies that microbes “[The] human microbiota might impact the efficacy of enediyne-based drugs and should be taken into consideration when developing new chemotherapies,” says Dr. Ben Shen, co-chair of The Scripps Research Department of Chemistry. “Future efforts to survey the human microbiome for resistance elements should be an important part of natural product-based drug discovery programs.”
in the gut could then pass these proteins on to their human hosts, thereby conferring drug resistance.

“These findings raise the possibility that the human microbiota might impact the efficacy of enediyne-based drugs and should be taken into consideration when developing new chemotherapies,” he added. “Future efforts to survey the human microbiome for resistance elements should be an important part of natural product-based drug discovery programs.”

Swiss Biotech T3 is exploring ways to harness engineered bacteria to trigger the immune system “by delivering selected human proteins directly into cells of the tumor microenvironment.”

A different kind of delivery
Scripps isn’t the only organization looking into the potential of bacteria. Swiss biotech T3 Pharmaceuticals received the “2018 Science Start-Up of the Year” award from Falling Walls Venture in the fourth quarter of the year for such work.

T3’s approach harnesses engineered bacteria to trigger the immune system “by delivering selected human proteins directly into cells of the tumor microenvironment,” the company explains. As noted in a Journal of Cell Biology article, “Bacteria have developed sophisticated nanomachines enabling the delivery of virulence proteins into eukaryotic cells (translocation). The type III secretion (T3S) system of certain gram-negative bacteria functions like a nanoyringe that injects substrate proteins into target cells.”

T3 notes that their approach is much faster than the current standard of DNA transfection, which “results in a heterogeneous and unsynchronized cell population after an incubation time of 12 to 48 hours. Hence, the protein under study is often present for far longer than physiologically relevant or desirable.” By harnessing the natural mechanisms of these bacteria, the company claims that they can offer “a fast, synchronized, homogenous and efficient protein delivery into almost all available cell lines.”

Putting T cells to work
Pairing drugs with antibodies to better direct them to tumors is a familiar concept, as seen by the rapid growth of the antibody-drug conjugate market. And recent work out of the Massachusetts Institute of Technology (MIT) is echoing that concept of effective pairings, but with a twist—rather than attaching drug payloads to antibodies, a research team has found a way to attach drugs to T cells.

T cells, lymphocytes that play a major role in the immune system’s response to cancer or infections, are one of the key cell types.

LONDON—In news from Cancer Research UK, it seems that restricting the ability of cancer cells to metabolize sugar could make oncolytic viruses more effective at attacking them, at least according to results described in a study published recently by the journal Cancer Research.

As Cancer Research UK notes, viruses that are trained to attack cancer cells—known as oncolytic viruses—can kill tumors without affecting healthy cells nearby. They normally work by invading the cells, multiplying and destroying the tumor from inside, and variations of them are being tested in clinical trials now.

In this new study, a team of scientists exposed lung, ovarian and colon cancer cells—as well as mouse models—to conditions similar to those in the human body, and investigated how manipulating cell metabolism can make cancer more vulnerable to oncolytic viruses.

In the lab, scientists usually keep cells at the perfect temperature and provide them with lots of glucose, as it’s easier to grow and store them this way. In this study, the researchers changed the lab conditions to make them reflect what actually happens in the human body, where sugar levels are much lower.

They found that oncolytic viruses worked better when less glucose was available. To investigate whether they could make the virus work even harder, the researchers then used a drug to restrict the cancer cells’ ability to metabolize sugar (its energy source) to see if this optimized the virus’ cancer killing capability.

They found that reducing sugar levels allowed the virus to multiply much faster, making treatment more effective and destroying cancer quicker.

“Our research in the lab showed that restricting the amount of sugar available to cancer cells makes these cancer-attack ing oncolytic viruses work even better,” said Arthur Dyer, lead author and Cancer Research UK-funded Ph.D. student from the University of Oxford. “We already know that this virus is effective against cancer—and this sugar-starving technique is a way to make it even better.”

This approach may also improve how potential cancer drugs are investigated in the lab.

Added Dyer: “When studying any kind of drug in the lab, we keep the cells in very high sugar conditions; it’s a bit like soaking them in Lucasade. But this doesn’t reflect the conditions that these cells would be exposed to in the body, which are normally much poorer—in cancer, they’re even worse because tumors typically have poor circulation. Our approach is more realistic in mimicking the conditions in the human body, which ultimately may help us to better predict how patients will respond to drugs well before any trials are planned.”

However, the researchers caution that their early findings should not be misinterpreted by patients who are looking to optimize treatments.

“It’s important to remember that changing your diet is not enough to starve cancer cells of sugar,” stressed Prof. Len Seymour, Cancer Research UK-funded study author from the University of Oxford. “A lot of people think that carbohydrates are bad, but that’s not the case—we need them, and cutting out sugar won’t cure cancer. Because cancer gobbles up glucose so quickly, the cells are very vulnerable to attack from a drug that targets the sugar pathway. The same effect cannot be achieved by eliminating sugar from your diet.”

The team is aiming to test its glucose-limiting approach to improving oncolytic virus treatment in clinical trials to assess whether it could be successfully implemented in cancer patients.

“By making treatments work more effectively, we hope that patients will be able to see positive results faster than before,” concluded Dr. David Scott, Cancer Research UK’s director of discovery research. “The next step is to test whether this approach works in clinical trials, and to find out which cancers respond best.”

Imagining getting 300 antibody hits in 1/300 the time.

Like less than 3 months’ time. It’s true. This revolutionary library, available to our clients through an exclusive partnership with Distributed Bio, makes fast, high volume antibody discovery a reality.

Working with Charles River’s discovery biology, pharmacology, and safety assessment expertise means you can take your qualified hits all the way through to IND for seamless, efficient discovery.

Find out what we can do for you at www.criver.com/antibody.
Researchers at the Massachusetts Institute of Technology are exploring a method to attach drugs to T cells as a way of attacking tumors.

**CANCER**

**CONTINUED FROM PAGE 21**

researchers are working to harness in better targeting cancer. By re-equiping the immune system to bypass cancer’s defenses, rather than trying to overpower it with higher doses of drugs, cancer treatment is more targeted and has fewer side effects.

Adoptive T cell therapy has emerged as a way to harness the immune system against tumors. Tumor-specific T cells are taken from a tumor, grown and expanded, then returned to the patient, or else circulating T cells are taken from the blood, modified to target proteins expressed on the surface of tumors, and then reintroduced to the patient’s system.

Dr. Darrell Irvine’s lab has been working on this approach for years, having reported a method in 2010 for attaching liposomes with cytokine payloads to tumor-specific T cells. There were drawbacks, however, in the form of a hard limit on how much of a payload the cytokines could carry, and their tendency to release the drug as soon as they were injected.

“This is based on the fact that although STAT3 inhibition could be achieved, it occurred via a mechanism that appears to be unique in its ability to inhibit STAT3 from upstream signaling, not directly from within the cancer cell itself. WP1066 appears to be very promising based on the preclinical data we have seen with this compound,” said Irvine, a professor of biological engineering and of materials science and engineering, a member of MIT’s Koch Institute for Integrative Cancer Research, and senior author of the study.

“When tested in mouse models with T cells designed to express a T cell receptor targeting a protein common in melanoma tumors, the tumors disappeared in roughly 60 percent of the mice. Similar effectiveness was seen in models with engineered glioblastoma cells. In addition, with the IL-15 linked to the gel nanoparticles, they were able to administer eight times as much of the therapeutic with no side effects.

The clinical trials for this approach are being performed by Torque Biotherapeutics, of which Irvine is a co-founder. In a recent press release detailing the presentation of preclinical data at this year’s AACR meeting, Dr. Thomas Andresen, chief scientific officer of Torque, reported that “Both IL-15 and IL-12 are potent cytokines capable of inducing strong antitumor immune responses, yet their clinical use as systemic therapies is limited by the potential for severe toxicities. Anchoring these powerful immune activators to the surface of T cells that traffic to tumors is a unique approach to direct immune power in the tumor microenvironment.”

Dr. Thomas Andresen of Torque Biotherapeutics

administration of these same cytokines and are the foundation for the first clinical trials that will begin later this year for Deep IL-15.

**From HIV to breast cancer**

Also in November, CytoDyn Inc. filed an Investigational New Drug application with the FDA for a Phase I/II clinical trial of PRO 140 (eribulin) in patients with metastatic triple-negative breast cancer. PRO 140 is a CCR5 antagonist being investigated by CytoDyn in HIV infection, given its connection with CCR5. By masking CCR5, HIV (R5) subtype is barred from entering and infecting healthy T cells.

However, CCR5 plays a part in tumor metastasis and immune signaling as well, and works to direct the flow of immune cells to inflamed sites. In terms of cancer, increased expression of CCR5 is a warning sign for several cancers, as it supports tumor invasion and metastasis, and CCR5 inhibitors have proven capable of blocking metastases in lab and animal models of breast and prostate cancer. Given that, CytoDyn is further exploring PRO 140 in cancer as well as HIV, with the intent of launching clinical trials in metastatic triple-negative breast cancer this year.

According to Dr. Richard Pestell, CytoDyn’s interim chief medical officer, “My previous study of 2,200 patients showed potential to have a positive effect in other types of metastatic cancers. We look forward to detailing the protocol for this trial following the FDA review period.”

**A new ‘buzz’ in glioblastoma**

One of the most unusual approaches in this collection of news is based on bees. Molecu- lin Biotech Inc. recently launched a Phase 1 clinical trial of WP1066 in glioblastoma. The small-molecule drug candidate is derived from the active ingredient in propolis, which is produced by honey bees. WP1066 inhibits STAT3, a cell signaling protein that plays a role in cell growth and proliferation, tumor angiogenesis, tumor development and immune response trigger- ing. STAT3 also helps tumors cells to evade the immune system and metastasize to secondary locations.

“Treating the first brain tumor patient with WP1066 is the start of a very exciting and encouraging program for doctors treating the worst types of brain cancers. There has been very little progress in recent years toward improved therapies for glioblastoma and other aggressive primary or metastatic brain tumors. WP1066 has shown extremely promising results based on animal studies where we have seen inhibition of tumor growth and improvements in survival,” said Dr. Sandra Silberman, a world-renowned oncologist and Molecu- lin’s chief medical officer. “This is based on the fact that although STAT3 has long been identified as an impor- tant target for treating tumors, for years most efforts have focused on attempts to indirectly inhibit STAT3 from upstream signaling, not from within the cancer cell itself. WP1066 appears to be unique in its ability to inhibit and in animal models to consistently and directly inhibit the activated form of STAT3 and pro- duce significant anticancer effects, including tumor growth inhibition and increased life span of treated animals.”

**Molecular in vivo**

Molecular in vivo

**Molecular in vivo**

“*My previous study of 2,200 patients showed that more than 50 percent of all breast cancers overexpress CCR5, and more than 90 percent of patients with triple-negative breast cancer re-expressed CCR5 selectively on their cancer. PRO 140, which has been shown as very safe without any reported drug-related serious adverse events in more than 620 patients, binds avidly to CCR5 on human breast cancers.*”

Dr. Richard Pestell, interim CMO of CytoDyn
Establishing immunotherapy for pediatric liver cancer

HOUSTON—As part of a $6-million effort to establish new therapies for high-risk pediatric liver cancer, Navin Vardarajan, associate professor of chemical and biomolecular engineering at the University of Houston, will modify T cells to recognize and kill glycamin-3, a molecule found in liver cancer cells.

With two previous awards from the Cancer Prevention & Research Institute of Texas (CPRIT), Vardarajan is working to improve effectiveness of T cell immunotherapy. On this CPRIT multi-investigator research award, he joins Andras Hecezy, a physician researcher at Baylor College of Medicine, in examining one of the most common forms of liver cancer in adolescents: hepatocellular (HCC) carcinoma. HCC patient survival rates are under 30 percent.

No effective cure is available for most metastatic hepatocellular tumors. Current treatment includes surgical resection or liver transplantation in combination with dose-intensive chemotherapy regimens. T cell-based immunotherapy has worked in other types of cancers, like leukemia and lymphoma. The team at Baylor will isolate the T cells and modify them with synthetic receptors, and then Vardarajan will get to work.

“We have a platform for documenting how well T cells work, and we will use it to determine which T cell properties are essential in fighting the cancer cells,” said Varadarajan, whose team built the microscopy-based methods for monitoring cellular function.

“We have a platform for documenting how well T cells work, and we will use it to determine which T cell properties are essential in fighting the cancer cells.”

Navin Vardarajan of the University of Houston

Once determined, certain functions can be added or subtracted through genetic editing to make the T cell the best cancer fighter possible. The modified cells will deliver targeted and tailored therapy in clinical trials at Baylor.

“The hope is to get consistent and durable patient responses in pediatric HCC by using the power of immunotherapy,” said Varadarajan, who credits CPRIT with the steps forward in immunotherapy. “Texas taxpayers are amazing for funding CPRIT. Much of this research would not be possible without it.”

A new neutropenia option for chemotherapy patients

NEW YORK—Despite increasing efforts to minimize the off-target damage of cancer treatments, most drugs come with side effects. One of the more common issues, particularly with chemotherapy, is neutropenia, when individual's counts of neutrophils (white blood cells) are drastically low. The condition makes patients vulnerable to infection, which puts a strain on patients' already weakened immune systems. BeyondSpring Inc. has shared clinical data on Plinabulin, its asset for preventing chemotherapy-induced neutropenia (CIN), that it points to it potentially standing as a better option than a current gold-standard neutropenia therapy.

While Neulasta, a current standard, is meant to activate the bone marrow to encourage the body to produce neutrophils, “Clinical data suggest that a large proportion of these neutrophils appear to represent immature neutrophils, which typically make their way to the tumor tissue, and tip the immune balance in the tumor into an immune-suppressive microenvironment,” BeyondSpring explains.

“While both Plinabulin and Neulasta monotherapy demonstrated equal effects in the prevention of CIN in terms of how often and how long patients experienced severe neutropenia in Study 105, this added demonstration of a potentially superior immune profile over Neulasta has distinct advantages. We now recognize the importance of our immune system in fighting cancer, and the avoidance of suppression of our immune system has the potential to result in better cancer outcomes and prognosis. A leading trend is to combine immunotherapy with chemotherapy, and the latter is known to induce CIN. With immune/chemotherapy combination, Plinabulin has the potential to offer advantages over Neulasta and G-CSFs in general for the prevention of CIN, to enable the best possible immune therapeutic efficacy,” said Dr. Ramon Mohanlal, executive vice president and chief medical officer at BeyondSpring.

In a study of patients with non-small cell lung cancer, Plinabulin proved comparable to Neulasta. When examining NLR (Neutrophil-to-Lymphocyte Ratio) and LMR (Lymphocyte-to-Monocyte Ratio), “Plinabulin did not show NLR > 5 or LMR < 3.2 values. Pro-myelocytes or myelocytes were observed in 77 percent of patients given Neulasta, compared to 14 percent of patients given Plinabulin (p < 0.001), and neutrophil bands were observed in more than 25 percent of patients given Neulasta, compared to 6% of patients given Plinabulin (p < 0.03),” according to a company press release. BeyondSpring added that “NLR values of > 5 and LMR values of < 3.2, as well as immature neutrophils, are associated with immune suppression and poor cancer prognosis.”

“Not only does Plinabulin appear to have immune-enhancing anti-cancer potential, but there is growing evidence supporting a superior product profile for the prevention of CIN. We previously reported a bone pain benefit with Plinabulin over Neulasta. Plinabulin prevents not only chemotherapy-induced neutropenia, but also immune/chemotherapy-induced thrombocytopenia. This new observation of avoidance of an immune suppressive potential as was observed with Neulasta adds to the list of differentiating features observed in clinical trials to-date for Plinabulin and sets the stage for Plinabulin as a novel CIN treat ment with potential for a superior product profile,” commented Dr. Lan Huang, CEO and co-founder of BeyondSpring.

“Neural recognition of the importance of our immune system in fighting cancer, and the avoidance of suppression of our immune system has the potential to result in better cancer outcomes and prognosis.”

Dr. Ramon Mohanlal of BeyondSpring

TELIX AND NIHON COLLABORATE ON ACTINUM CANCER THERAPEUTICS

MELBOURNE, Australia & TOKYO—Telix Pharmaceuticals Ltd., a clinical-stage biopharmaceutical company focused on the development of diagnostic and therapeutic products based on targeted radiopharmaceuticals or “molecularly-targeted radiation,” and Nihon Medi-Physics Co., Ltd. (NMP), a manufacturer and supplier of radiopharmaceuticals and related products in Japan, have announced the signing of a collaboration agreement to jointly evaluate the feasibility of 225Ac-labeled (actinium) antibodies for the treatment of clear-cell renal cell cancer (ccRCC).

In order to materialize therapeutics (a concept of integrating therapeutics and diagnostics), NMP is actively developing an alpha-emitting radionuclide (such as 212Pb)-based therapeutic pipeline, following the decision to build a new R&D site to produce radionuclides including 225Ac. In comparison to other types of radionuclides, alpha-emitters have relatively higher energy to damage cancer cells and shorter energy deposit range to minimize damages to the peripheral normal cells. Therefore, 225Ac, an alpha-emitting nuclide, is expected to have significant clinical potential for the treatment of cancer via nuclear medicine techniques. The parties will collaborate to apply NMP’s novel linker chemistry to Telix’s anti-CAIX antibody and jointly conduct proof-of-concept studies.

“Part of the attractiveness of this collaboration with NMP is that Telix’s 89Zr-girentuximab (TLX250) PET imaging tracer also targets CAIX, and can therefore select patients for therapy,” said Dr. Shintaro Nishimura, Telix Pharmaceuticals’ Japan president. “Through this important collaboration with NMP, we hope to materialize therapeutics a reality in Japan.”

Added NMP President Hisashi Shimoda: “NMP views theranostic radiopharmaceuticals as a growth driver for our business. This collaboration with Telix, who is extensively developing products in the oncology field, is expected to impact positively on our business strategy. NMP has long-standing experience and skills in the manufacture and supply of radiopharmaceuticals, and Telix’s product portfolio, combined with our expertise, will together contribute greatly to moving closer toward the real theranostics.”

For more information, visit www.DDN-News.com
IMV moves to develop DPX-Survivac as monotherapy for recurrent ovarian cancer

DARTMOUTH, Nova Scotia—IMV Inc., a clinical-stage immuno-oncology company, announced in mid-November an amendment to its Phase Ib/2 clinical trial evaluating the safety and efficacy of IMV’s lead candidate, DPX-Survivac, in combination with either 100 mg or 300 mg of epacadostat in patients with recurrent ovarian cancer.

A review of new data from the Phase Ib portion of the clinical trial demonstrates a high response rate and a durable clinical benefit in a subpopulation of patients with a clinical marker predictive of a response to DPX-Survivac and correlated to its novel mechanism of action. New data include:

Efficacy signals in the subpopulation of patients who received 100 mg dose epacadostat included 100-percent tumor regressions and 100-percent disease control rate; and 80 percent of these patients reached a best response of a partial response.

Long duration of clinical benefit observed in responders with a median duration of 590 days, including one patient that has passed the two-year mark without disease progression.

Clinical benefit correlated to DPX-Survivac’s MOA and clinical study primary endpoints: surviving specific T cells in the blood and T cell infiltration into tumors.

The safety profile of DPX-Survivac is consistent with the profile observed in the company’s previously reported studies.

Based on 300 mg cohort results, IMV and Incyte have agreed to stop dosing patients with epacadostat. IMV will continue the Phase Ib/2 trial as a monotherapy study evaluating DPX-Survivac in the recurrent ovarian cancer subpopulation. IMV will inform and work with investigators appropriately modify the study in a manner consistent with the best interests of each patient.

IMV and Incyte will continue to evaluate the potential of additional combination studies.

“The goal of the trial was to evaluate combination therapies. However, the new data indicate that DPX-Survivac shows activity as a monotherapy in late-stage patients, which can potentially translate into clinical benefit,” said Frederic Ors, CEO of IMV. “In parallel to the amended monotherapy trial, we will continue to investigate other combinations with our lead product candidate as we continue our work to deliver new immunotherapy options that may benefit more patients in multiple cancers.”

“We are very pleased that the Phase Ib trial results to date validate the mechanism of action of DPX-Survivac, helping us to identify patients more likely to benefit from our drug candidate,” added Dr. Gabriela Nicola Rosu, chief medical officer at IMV. “Identifying which patients have the greatest potential for responding to a drug candidate is key for the success of immunotherapy clinical trials, and we look forward to continued work with investigators and trial sites to advance the study of DPX-Survivac to help address the significant unmet medical needs of these patients.”

Interim data supports combination therapy in multiple cancer types

TOKYO—This year’s annual meeting for the Society for Immunotherapy of Cancer saw Eisai Co. Ltd. and Merck & Co. Inc., known as MSD outside of the United States and Canada, share data regarding a combination regimen of Eisai’s Lenvima (lenvatinib) and Merck’s Keytruda (pembrolizumab). The combination therapy was tested in three types of metastatic cancer, including non-small cell lung cancer (NSCLC), melanoma and urothelial carcinoma.

Though the companies presented only interim analysis data, the two therapies were generally well tolerated in all three indications. In addition, they saw “encouraging antitumor activity,” according to a company press release.

In a Phase Ib/2 trial of Lenvima and Keytruda in patients with metastatic NSCLC, the primary endpoint—objective response rate at week 24 per immune-related RECIST (irRECIST)—was 33.3 percent. Median progression-free survival per irRECIST was 5.9 months, with a progression-free survival rate at 12 months per irRECIST of 29 percent. The median duration of response (DOR) was 10.9 months.

Though the combination was generally well tolerated, there were some adverse events. Ten patients (8 percent) in the NSCLC cohort saw Grade 3 treatment-related adverse events (TRAEs), with one patient (5 percent) experiencing Grade 4 TRAEs and one treatment-related death. The most common adverse events of any grade were decreased appetite, proteinuria, hypertension, fatigue, hypothyroidism, diarrhea and arthralgia. These were common in the other two combination cohorts as well, with the melanoma cohort also seeing cases of dysphonia. In addition, the entirety of the melanoma arm experienced at least one TRAE, though there were no treatment-related deaths.

In the patients with metastatic melanoma, researchers saw an objective response rate (ORR) at week 24 per irRECIST of 47.6 percent, with median PFS of 5.5 months and a PFS rate at 12 months of 34.7 percent. Median DOR was recorded as 12.5 months.

The urothelial carcinoma arm featured 20 individuals who were either treatment-naïve or who had received up to two prior lines of therapy. In terms of the primary endpoint, ORR at week 24 per irRECIST in this cohort was 25 percent. In terms of secondary end-points, the interim results reported median PFS of 5.4 months. Like the NSCLC cohort, this arm of the trial also saw one treatment-related death.

“We are increasingly confident that these interim analyses of new clinical trial data on the combination of Lenvima and Keytruda in non-small cell lung cancer, melanoma and urothelial cancer continue to verify the potential of this combination,” said Dr. Takashi Owa of the Oncology Business Group at Eisai

Keytruda from U.S.-based Merck & Co. (pictured here) is being tested in combination with Japan-based Eisai’s Lenvima.

patients in need of new treatment options as soon as possible.”

These studies fall under an agreement established by Eisai and Merck & Co. in March to co-develop and co-commercialize Lenvima at both a monotherapy and in combination with Keytruda. Beyond the studies that are already underway, the partners will also conduct clinical studies investigating the combination regimen of Lenvima and Keytruda in 11 potential indications covering six types of cancer—bladder cancer, endometrial cancer, head and neck cancer, hepatocellular carcinoma, melanoma and NSCLC—as well as a basket trial featuring six other subtypes of cancer. **
Forward momentum for Nkarta

LA JOLLA, Calif.— In one of the latest efforts toward developing a cancer vaccine, Scripps researchers have engineered a vaccine capable of working synergistically with additional therapeutics.

By adding the adjuvant Diprovocim, a toll-like receptor TLR1/TLR2 agonist, to a cancer vaccine, the research team saw a significant difference in survival rates. In mice with aggressive melanoma who had been treated with anti-PD-L1, the mice that received the cancer vaccine and Diprovocim saw a 100-percent survival rate over 54 days. By comparison, 0 percent of mice who received only the vaccine survived, while 25 percent survived in the cohort that received the vaccine and an adjuvant known as alum.

According to their research, the addition of Diprovocim supported the vaccine by stimulating the production of tumor-infiltrating leukocytes. In the mice who had received Diprovocim and the vaccine, attempts to re-challenge their systems with the melanoma tumors failed. As noted in the study’s abstract, “Diprovocim-adjuvanted ovalbumin immunization promoted antigen-specific humoral and CTL responses and synergized with anti–PD-L1 treatment to inhibit tumor growth, generating long-term antitumor memory, curing or prolonging survival of mice engrafted with the murine melanoma B16-OVA. Diprovocim induced greater frequencies of tumor-infiltrating leukocytes than alum, of which CD8 T cells were necessary for the antitumor effect of immunization plus anti–PD-L1 treatment.”

“This co-therapy produced a complete response—a curative response—in the treatment of melanoma,” summarized Scripps Research’s Dr. Dale Boger, who co-led the study with Nobel laureate Dr. Bruce Beutler of UT Southwestern.

Moving forward, the team intends to explore the vaccine design further and test it with cancer therapeutics besides anti-PD-L1.

The more, the merrier

LA JOLLA, Calif.— In one of the latest efforts toward developing a cancer vaccine, Scripps researchers have engineered a vaccine capable of working synergistically with additional therapeutics.

By adding the adjuvant Diprovocim, a toll-like receptor TLR1/TLR2 agonist, to a cancer vaccine, the research team saw a significant difference in survival rates. In mice with aggressive melanoma who had been treated with anti-PD-L1, the mice that received the cancer vaccine and Diprovocim saw a 100-percent survival rate over 54 days. By comparison, 0 percent of mice who received only the vaccine survived, while 25 percent survived in the cohort that received the vaccine and an adjuvant known as alum.

According to their research, the addition of Diprovocim supported the vaccine by stimulating the production of tumor-infiltrating leukocytes. In the mice who had received Diprovocim and the vaccine, attempts to re-challenge their systems with the melanoma tumors failed. As noted in the study’s abstract, “Diprovocim-adjuvanted ovalbumin immunization promoted antigen-specific humoral and CTL responses and synergized with anti–PD-L1 treatment to inhibit tumor growth, generating long-term antitumor memory, curing or prolonging survival of mice engrafted with the murine melanoma B16-OVA. Diprovocim induced greater frequencies of tumor-infiltrating leukocytes than alum, of which CD8 T cells were necessary for the antitumor effect of immunization plus anti–PD-L1 treatment.”

“This co-therapy produced a complete response—a curative response—in the treatment of melanoma,” summarized Scripps Research’s Dr. Dale Boger, who co-led the study with Nobel laureate Dr. Bruce Beutler of UT Southwestern.

Moving forward, the team intends to explore the vaccine design further and test it with cancer therapeutics besides anti-PD-L1.

There are many access points for news and knowledge of the world of oncology therapeutics R&D and diagnostics, but in your multitude of choices, don’t overlook DDNews’ Cancer Research News site. Both overlapping with and distinct from the main DDNews website, Cancer Research News provides a doorway to news of those making strides in cancer drug development, from individual groundbreaking scientists to big-name companies; a gateway to recent research studies and academic efforts in oncology; and a pathway to find pointed commentaries on issues related to cancer therapeutics and diagnostics.

Visit www.ddncancer.com today and every day you need to know more about the world of oncology.
**New combo therapy for pancreatic cancer?**

Pairing investigational peptide with Keytruda yields promising results for BioLineRx

**BY KRISTEN SMITH**

TEL AVIV, Israel—BioLineRx, a drug development company specializing in oncology and immunology, recently released results of a study pairing its BL-8040 peptide with Keytruda (pembrolizumab) from Merck & Co. (known as MSD outside the United States and Canada) as a potential treatment for metastatic pancreatic cancer. The results, reported at the European Society for Medical Oncology (ESMO) meeting recently, indicate that the COMBAT/KEYNOTE-202 study data show promising results in disease control and overall survival for patients in the trial.

According to principal investigator Dr. Manuel Hidalgo, a professor of medicine at Harvard Medical School and co-director of the Pancreatic Cancer Research Program at Beth Israel Deaconess Hospital, pancreatic cancer is one of the most difficult cancers to treat.

“Pancreatic cancer remains an area of very high unmet medical need, as currently approved treatments are limited by poor response rates and survival,” he stated. “Recent advances in cancer treatment with immune checkpoint inhibitors in many tumor types, pancreatic cancer remains refractory to these treatment options.”

BioLineRx scientists have been developing a novel short peptide called BL-8040 because of its efficacy as a high-affinity antagonist for CXCR4, the most widely expressed chemokine receptor in human cancers. Specifically, in pancreatic cancer, high CXCR4 expression levels correlate with poor prognosis, contributing to the promotion of tumor growth, invasion, survival, angiogenesis, and metastasis. In previous clinical trials, BL-8040 successfully mobilized immune cells to induce direct tumor cell death. In addition, clinical findings have demonstrated the ability of BL-8040 to mediate infiltration of T cells into tumors that were previously immunologically “cold” and devoid of immune cell infiltrate.

In January 2016, BioLineRx entered into an immunotherapy collaboration with Merck and initiated the COMBAT/KEYNOTE-202 study to test the hypothesis that combining BL-8040 with immune checkpoint blockade would increase the responsiveness of pancreatic cancer patients to immunotherapy. The Phase 2a study launched with 37 patients with metastatic pancreatic adenocarcinoma. The study data indicates that the BL-8040...
BL-8040
CONTINUED FROM PAGE 26
combination therapy is safe and well tolerated, with demonstrated antitumor effect not seen using Keytruda alone.

According to Dr. Abi Vainstein, vice president of clinical and medical affairs at BioLineRx, the results are promising. “[Our] findings demonstrate the ability of BL-8040 to change the tumor microenvironment by increasing infiltration of tumor-reactive T cells and decreasing myeloid suppressive T cells. In addition, the results showed that the combination of BL-8040 with Keytruda elicits real clinical activity. These results were very encouraging for us, as the BL-8040/Keytruda combination demonstrated promising impact (especially in second-line patients) and the role of BL-8040 in the treatment of stage IV pancreatic cancer, one of the ‘coldest’ tumors there is.”

The researchers are looking ahead to the next phase in testing, by adding chemotherapy to the combination. Chemotherapy has been shown to reduce overall tumor burden while inducing immunogenic cell death, leading to activation and expansion of new tumor reactive T cells. This suggests adding it to this cocktail may have even better therapeutic value. Regulatory submissions required to conduct the additional arm of the study have been made, and its initiation is planned for the fourth quarter of 2018. “We believe BL-8040 can further facilitate the infiltration of these T cells into the tumor core, alongside the restoration of T cell activity within the tumor by Keytruda,” says Philipp Serlin, CEO of BioLineRx. “We look forward to commencing the triple-combination arm of this important study by the end of this year, with results expected by the end of 2019.”

In other recent news, BioLineRx announced that the U.S. Food and Drug Administration (FDA) has granted the Biological Product Designation for AGI-134, the company’s novel immunotherapy compound, which is currently in the early stages of a Phase 1/2a study in solid tumors. Said Serlin in early November, reporting on the company’s quarter one performance and financials. “We made significant progress during the third quarter and subsequent period advancing clinical development of both of our oncology programs—BL-8040 and AGI-134. The contiguity of the combination of both of our oncology programs has been shown to reduce overall survival (mOS) of 17.8 months, compared to 6.4 months mOS for patients who received PD-1 inhibitors. The immunologic mechanism of action of IL-12 is to activate and expand T cells, which is likely responsible for the improved survival associated with Controlled IL-12 used as monotherapy in patients with GBM. Biopay data also revealed upregulation of immune checkpoints providing what Ziopharm deems “compelling rationale” for combining with PD-1 inhibitors. The immunologic mechanism of action of IL-12 is likely the reason elevated doses of steroids may reduce its activity. Phase 3 GENESIS study in stem-cell mobilization is now advancing in the randomized, placebo-controlled, part two of the trial. We are also rapidly moving forward in our expanded collaboration with Merck in pancreatic cancer, on the basis of the encouraging results recently presented at ESMO, with an additional cohort adding chemotherapy to the BL-8040/Keytruda combination. Further, we are very pleased to have initiated the first-in-human clinical study for AGI-134, our unique immunotherapy cancer vaccine. These achievements follow BL-8040’s very promising results in relapsed/refractory AML that were presented at the recent EHA Congress during the second quarter, showing significantly improved overall survival compared to historical data.”

Ziopharm provides update on Controlled IL-12 platform at Society for Neuro-Oncology meeting

By DDNews Staff

BOSTON—Ziopharm Oncology Inc. in mid-November provided an update on its Controlled IL-12 platform following a presentation of positive data from its Phase 1 clinical trial in recurrent glioblastoma (rGBM) at the Society for Neuro-Oncology (SNO) annual meeting in New Orleans.

Ziopharm is developing Controlled IL-12—or Ad-RTS-hIL-12 plus veledimex, a gene therapy that controls the expression of interleukin 12 (IL-12)—for the treatment of rGBM as both a monotherapy and in combination with immune checkpoint inhibitors. The company is driving this platform forward to secure a development partner in support of registrational trials.

Phase 1 data have shown that Ad-RTS-hIL-12 with a 20 mg dose of veledimex and less than 20 mg of the steroid dexamethasone is the preferred dosing regimen to treat patients with rGBM. When treating patients with Ad-RTS-hIL-12 plus veledimex, higher doses of steroids appear to suppress the immune response and negatively affect survival compared to low-dose steroids.

Ziopharm has enrolled 15 patients in an expansion of its Phase 1 trial designed to further evaluate preferred dosing of Ad-RTS-hIL-12 with 20 mg of veledimex as monotherapy with guidance on minimizing the dose of steroids. This expansion cohort for this study, which was initiated in the third quarter of 2018, is accruing rapidly and is expected to be fully enrolled with at least 25 patients in the first quarter of 2019. The company is advancing Controlled IL-12 as a combination therapy with PD-1 inhibitors, and is enrolling the second dosing cohort in a Phase 1 trial to evaluate Controlled IL-12 in combination with the PD1 inhibitor Opdivo (nivolumab). If all goes to plan, Ziopharm expects to begin a Phase 2 trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with Regeneron Pharmaceuticals’ PD-1 antibody Libtayo (cemiplimab-rwju) in the first half of 2019.

Ziopharm has enrolled more than 100 patients with Ad-RTS-hIL-12 plus veledimex and administered more than 1,200 doses of veledimex across three types of solid tumors, building what it calls “a significant safety profile and mechanistic dataset.” Biopay data reportedly demonstrated that Controlled IL-12 turns immunologically “cold” tumors “hot” based on sustained infiltration of killer T cells, which is likely responsible for the improved survival associated with Controlled IL-12 used as monotherapy in patients with GBM. Biopay data also revealed upregulation of immune checkpoints providing what Ziopharm deems “compelling rationale” for combining with PD-1 inhibitors. The immunologic mechanism of action of IL-12 is likely the reason elevated doses of steroids may reduce its activity.

Positive data for brain cancer treatment

By DDNews

Data presented at SNO 2018 were generated from the company’s Phase 1 monotherapy trial, which evaluates two methods of administration of Ad-RTS-hIL-12, explores the dosing of veledimex and evaluates the impact of steroids. Ad-RTS-hIL-12 plus veledimex continues to be well tolerated, according to Ziopharm, with related adverse events reversible across all cohorts upon stopping the oral administration of veledimex. A sub-analysis of patient data in the 20 mg veledimex monotherapy cohort shows that reduced dosing of the steroid dexamethasone had a positive impact on survival compared to higher doses in patients that received Controlled IL-12 via carotid or stereotactic injection. Six patients who received 20 mg or less of dexamethasone cumulatively over 15 days had median overall survival (mOS) of 17.8 months, compared to 6.4 months mOS for patients who received more than 20 mg of dexamethasone during the same observation period. The entire cohort of 15 patients that received 20 mg veledimex had mOS of 12.7 months with a mean follow up of 15.1 months. These data, Ziopharm says, support continued development of Controlled IL-12, especially considering the benchmark mOS of five to eight months for patients with rGBM that serves as historical controls.

“Glioblastoma at recurrence is a dreadful cancer with few treatment options that have demonstrated success. These updated data show a promising extension of patients’ survival and demonstrate how controlling the powerful cytokine IL-12 can engage the body’s own immune system to generate an antitumor response against rGBM.”

Dr. Antonio Chiocca of Harvard Medical School and Dana-Farber Cancer Institute

“These updated data show a promising extension of patients’ survival and demonstrate how controlling the powerful cytokine IL-12 can engage the body’s own immune system to generate an antitumor response against rGBM.”

Dr. Antonio Chiocca of Harvard Medical School and Dana-Farber Cancer Institute

For more information, visit www.DDN-News.com
“The DCE technology platform selectively replaces certain hydrogen atoms with deuterium to provide, in favorable cases, better pharmacokinetic or metabolic properties, and thereby enhances clinical safety, tolerability or efficacy,” Tung explained. “While deuterium substitution has the potential to alter a compound’s metabolism in humans, now demonstrated in a number of clinical studies, it typically does not alter its potency, selectivity or general physical or chemical properties. As a result, when a drug is known to provide pharmacological benefits in humans, we have high confidence that the deuterium-substituted compound will provide similar actions. This often allows us to determine proof of concept for our technology in early-stage clinical evaluation (Phase 1) rather than waiting for later-stage trials to see if the compound has promise as a drug.”

He added, “We are hoping to find a cure for this devastating and poorly treated autoimmune disease. AA, a chronic condition, affects women, men and children of all ages. The disease profoundly impacts patients, and there are no FDA-approved treatment options to date. CTP-543 has the potential to be the first FDA-approved oral treatment for alopecia areata. We have generated the first double-blind, placebo-controlled, dose-ranging data demonstrating its effect in hair regrowth and its associated safety profile.”

The FDA has granted Fast Track designation for CTP-543, which was discovered by applying Concert’s deuterium chemistry technology to modify ruxolitinib, a drug that selectively inhibits Janus kinases 1 and 2 (JAK1 and JAK2). It is commercially available under the name Jakafi for the treatment of certain blood disorders. Deuterium modification of ruxolitinib was found to alter its human pharmacokinetics in ways that could enhance its use as a treatment for alopecia areata, according to Tung.

Concert was one of the first companies to utilize deuterium as a drug development tool, and has built a strong intellectual portfolio on deuterium substitution has the potential to alter a compound’s pharmacokinetic or metabolic properties, and thereby enhances clinical safety, tolerability or efficacy.”

Dr. Roger Tung, president and CEO of Concert Pharmaceuticals is aiming to be the first to deliver a cure for the autoimmune disease alopecia areata with its CTP-543 compound.

The DCE technology platform selectively replaces certain hydrogen atoms with deuterium to provide, in favorable cases, better pharmacokinetic or metabolic properties, and thereby enhances clinical safety, tolerability or efficacy.”

Against atrial fibrillation

GENETIC-AF Phase 2B AFB results presented at AHA 2018 meeting

BY DONNEWS STAFF

WESTMINSTER, Colo.—ARCA biopharma Inc., a biopharmaceutical company applying a precision medicine approach to developing genetically targeted therapies for cardiovascular diseases, in mid-November presented data from the atrial fibrillation burden (AFB) substudy of its Phase 2B GENETIC-AF clinical trial in a poster session at the American Heart Association (AHA) 2018 Scientific Sessions in Chicago. Presenting the data was Dr. Jonathan Pocicini, an associate professor of medicine and director of the Duke Center for Atrial Fibrillation at Duke University Medical Center.

GENETIC-AF was a Phase 2B, double-blind, superiority clinical trial evaluating Gencaro (bucindolol hydrochloride) as a genetically targeted treatment for atrial fibrillation (AF) in patients with heart failure and reduced left ventricular ejection fraction (HFpEF). Safety data indicated that Gencaro was generally safe and well tolerated in the AF/HFrEF population investigated, with a safety profile similar to the active comparator metoprolol succinate (Toprol XL).

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/ or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.

The primary endpoint results for the trial were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients also underwent continuous heart rhythm monitoring. In these analyses, a trend for benefit compared to Toprol XL for the endpoint of time to AF recurrence based on AFB. In this substudy, Gencaro demonstrated similar trends for benefit compared to Toprol XL for the endpoint of time to AF recurrence when measured by continuous monitoring with implanted devices and by intermittent ECG-based monitoring. Analyses were also presented for a cohort that excluded patients with long-standing (i.e., ≥2 years) and heavily pretreated HF and/or AF. In these analyses, a trend for benefit in favor of Gencaro over Toprol XL was observed in the overall population and in the AFB substudy population using device-based detection.
“The LOXL2 enzyme is involved in the cross-linking of collagen and elastin fibers in the body, and increased levels found in organs such as the lungs, liver, kidney and heart are strongly associated with fibrotic disease. A LOXL2 inhibitor blocks the enzyme and stops cross-linking happening.”

Gary J. Phillips, CEO of Pharmaxis

Pharmaxis announced positive results recently from a Phase 1 trial for its second LOXL2 inhibitor, which is aimed at fibrotic diseases like non-alcoholic steatohepatitis and idiopathic pulmonary fibrosis.

FIBROSIS

CONTINUED FROM PAGE 26

LOXL2 enzyme is involved in the cross-linking of collagen and elastin fibers in the body and increased levels found in organs such as the lungs, liver, kidney and heart are strongly associated with fibrotic disease. A LOXL2 inhibitor blocks the enzyme and stops cross-linking happening. The cross-linking of collagen and elastin driven by LOXL2 are the final stages in the fibrotic process that often starts with chronic inflammation that is driven by metabolic diseases such as diabetes.”

“There are a number of drugs in development to dampen the metabolic and inflammatory drivers of fibrosis, but there are very few effective options to treat fibrosis itself,” Phillips continues. “Many of these treatments may cause a slowing of disease progression but many researchers believe that combining one or more of these approaches with a drug that tackles the fibrotic process directly will be necessary to effect a real improvement in treatment of diseases like NASH and IPF.”

The Pharmaxis LOXL2 program compounds are highly selective small-molecule inhibitors of LOXL2 that can be administered orally, and the company’s preclinical development program supports the potential of both compounds to treat fibrotic disease in one or more organs. Phillips says, adding: “Pharmaxis believes that it has a best-in-class program, with no other LOXL2 inhibitors under development that can produce 24-hour reduction in LOXL2 from a single daily dose.”

The double-blind, placebo-controlled study consisted of two stages. The first single ascending dose stage was conducted in 48 healthy subjects divided into six groups, with each taking a single dose ranging from 5 mg to 200 mg, or placebo. The second multiple ascending dose stage was conducted in 24 healthy subjects divided into three groups. Each received a single daily dose of either 50 mg, 100 mg, 200 mg or placebo for 14 days.

Repeating the positive results seen in the Phase 1 trial of the first LOXL2 inhibitor compound announced on Oct. 10, the reportedly excellent drug-like properties demonstrated in earlier preclinical testing were confirmed. There were no adverse safety findings, and the pharmacokinetic profile showed the expected dose-related increases in exposure.

“The targeted inhibition of greater than 80 percent of the LOXL2 enzyme has now been demonstrated in blood serum by both compounds for a full 24 hours from a single dose over a 14-day period. The second compound achieved more than 85 percent inhibition over 24 hours from a 100mg daily dose compared to the 400mg dose required to reach this level for the first compound,” notes Phillips.

“Both compounds have met our objectives for safety and enzyme inhibition in the Phase 1 studies, but the different pharmacokinetic properties of the two compounds may also usefully lend themselves to application in different disease indications.”

“Several large Pharma companies are interested in the Pharmaxis program, where both of our LOXL2 inhibitors have now successfully completed Phase 1 studies and demonstrated a best-in-class profile with 24-hour inhibition of the target enzyme from a single daily dose,” Phillips says. “In a further significant scientific advancement, we have also managed to underline the relevance of the program to potential partners by using our proprietary research tools to confirm that our compounds directly inhibit the activity of the raised levels of LOXL2 seen in diseased tissue from NASH and IPF animal models.

“The compounds are undergoing three-month toxicity studies which are due to report in the current quarter. Pharmaxis is working on a parallel licensing deal for this asset and a number of companies are reviewing our scientific data package. Following the completion of the data package, Pharmaxis intends to conduct a final series of scientific briefings to potential partners before moving to commercial partnering discussions to secure a comprehensive licensing agreement in 2019.”

Arix Bioscience, a global health-care and life-sciences company supporting medical innovation, was pleased to note the positive results from the Phase 1 clinical trial. Arix Bioscience led the A$24 million (about $17.7 million in U.S. dollars) financing for Pharmaxis in August, acquiring an 11.1-percent equity stake. Arix’s Ed Rayner also joined the Pharmaxis board of directors in September 2018.

Pharmaxis hosted an investor research briefing on Nov. 20, providing an overview of the Pharmaxis drug discovery pipeline, including: an anti-inflammatory drug currently being developed with Boehringer Ingelheim; work in collaboration with the Garvan Institute of Medical Research on an antifibrotic LOX inhibitor targeting pancreatic cancer; and an antifibrotic LOXL2 inhibitor program currently completing Phase 1 trials and extended toxicity studies.

“Pharmaxis is also developing other compounds to inhibit all lysyl oxidase family members (LOX, LOXL1, 2, 3 and 4) and is making good progress in this area, which will focus initially on pancreatic cancer,” mentions Phillips. According to a news release also from Nov. 20, Pharmaxis has completed the preclinical package on its antifibrotic lysyl oxidase program focused on pancreatic cancer and filed an ethics submission to enable a Phase 1 clinical trial in healthy volunteers. The trial is planned to commence in the first quarter of 2019.

Pharmaxis is collaborating with the Garvan Institute of Medical Research to investigate the therapeutic potential of LOX inhibition in pancreatic cancer. Researchers at the Institute have evidence in mouse models that inhibition of the LOX family alters the tumor microenvironment, rendering tumors more susceptible to existing therapies. The team has also generated positive results in in-vitro and in-vivo models of pancreatic cancer using the Pharmaxis LOX inhibitor.

The Garvan Institute’s research on the role of LOX enzymes in pancreatic cancer and the potential of Pharmaxis compounds in this disease will be the subject of presentations at upcoming international scientific symposia in 2019. 
PORTLAND, Ore. & CAMBRIDGE, Mass.— HealthCan30 DDNEWS || DECEMBER 2018

are committed to providing tools to physicians and
desix," said David Brunel, CEO of Biodesix. “We

real-world environment, and a top priority for Bio-
desix. “We are committed to providing tools to physicians and

across the continuum of lung cancer care.”

the test so far indicate that it could reduce
unnecessary procedures by 40 percent by identify-
ing benign nodules, consequently also reducing
cost of care and patient anxiety. In the previous
PANOPTIC trial, BDX-XL2 identified likely benign
nodules with 97-percent sensitivity and 98-per-
cent high negative predictive value.

The ORACLE study is critical to understanding
how BDX-XL2 impacts treatment decisions in a
real-world environment, and a top priority for Bio-
desix,” said David Brunel, CEO of Biodesix. “We

have clarified
clinical trials
form of failed
research and development
and as such, there are “enormous
effects and improving their quality of life much sooner, "

so that physicians have the information needed to iden-
tify Tasigna capsules and who, after maintaining a
deep molecular response of MR4.5, may qualify
for treatment-free remission (TFR) and monitoring.

This is an encouraging milestone for the MRDx BCR-
ABL Test, enabling it to become more broadly acces-
sible to patients beyond the United States,” said
Dan Snyder, CEO of MolecularMD. “The test ensures
that physicians have the information needed to iden-
tify Tasigna-treated patients who meet the stringent
eligibility criteria to attempt TFR and provides the
robust sensitivity and accuracy necessary for mon-
toring minimal residual disease with confidence.”

BY JEFFREY BOULEY
SALT LAKE CITY—Recently, Myriad Genetics
Inc., which is focused on molecular diagnos-
tics and personalized medicine, announced
progress with the BRACAnalysis CDx on
two fronts: study results supporting its use
as a companion diagnostic with Lynparza
for ovarian cancer, and approval for its use
with Talzenna for HER2-negative metastatic
breast cancer.

The more recent news, coming late in
October, revealed that in the Phase 3
SOLO-1 trial, the test accurately identified
patients with newly diagnosed, advanced-
stage, BRCA-mutated (BRCAm) ovarian

"The ORACLE study is critical to understanding
how BDX-XL2 impacts treatment decisions in a
real-world environment, and a top priority for Bio-
desix,” said David Brunel, CEO of Biodesix. “We

company: the ORACLE study, the first study to eval-
uate the test in a real-world setting, was
achieved.

Leukemia remission test
gains regulatory clearance
PORTLAND, Ore. & CAMBRIDGE, Mass.—HealthCan-
da recently granted regulatory approval to Molec-
ularMD Corporation for its MRDx BCR-ABL Test, which
was cleared by the FDA in late 2017. The
quantitative diagnostic test is intended to help
monitor treatment with tyrosine kinase inhibi-
tors in patients with Philadelphia chromosome-
positive chronic myeloid leukemia, and to identify
patients in the chronic phase who are receiving
Tasigna capsules and who, after maintaining a
deep molecular response of MR4.5, may qualify
for treatment-free remission (TFR) and monitoring.

"This is an encouraging milestone for the MRDx BCR-
ABL Test, enabling it to become more broadly acces-
sible to patients beyond the United States,” said
Dan Snyder, CEO of MolecularMD. “The test ensures
that physicians have the information needed to iden-
tify Tasigna-treated patients who meet the stringent
eligibility criteria to attempt TFR and provides the
robust sensitivity and accuracy necessary for mon-
toring minimal residual disease with confidence.”

BY KELSEY KAUSTINEN

Companies continue efforts to develop
tests for early Alzheimer’s diagnosis

WHILE RECENT
setbacks in the form of failed
clinical trials have clarified
that it will be a longer road to
effective treatments for Alzhei-
mer’s disease (AD), those setbacks
donn’t dimmed optimism for
developing diagnostics for the
neurodegenerative disorder.

Since the dementia associated
with Alzheimer’s becomes notice-
able later in the course of the
disease, the need for earlier diag-
nostic options is clear. The total
cost of care for individuals with
Alzheimer’s or other dementias
in 2018 is estimated at $277 billion,
and as such, there are “enormous
cost savings, both financial and
emotional, that can be achieved
with an accurate diagnosis even
in the absence of a therapeutic,”
according to diagnostics company
NeuroDiagnostics LLC.

Digging in deep for diagnostics
Companies continue efforts to develop
tests for early Alzheimer’s diagnosis

BY KELSEY KAUSTINEN

Testing the waters in
genetic screening
Nonprofits co-fund feasibility study
to test screening tool for 75,000
newborns for Angelman, Prader-Willi,
fragile X and Dup15q syndromes

BY DDNEWS STAFF

AURORA, Ill. & WALNUT, Calif.–In early November, the
Angelman Syndrome Foundation and the Foundation
for Prader-Willi Research announced funding to support
the world’s largest newborn screening study for four rare
genetic disorders: Angelman, Prader-Willi, fragile X and
Dup15q syndromes. The Victorian Medical Research Accel-
eration Fund this year also contributed $100,000 toward
the project.

In a pilot study, David Godier—an associate professor at the
Murdoch Children’s Research Institute in Melbourne, Austra-
lia—will screen 75,000 newborns, establishing the feasibility
of the test for large-scale screening.

“Newborn screening means families with loved ones with
Angelman, Prader-Willi, fragile X and Dup15q syndromes
will find a diagnosis in weeks instead of years, avoiding a
painful diagnostic journey. And, if we can diagnose indi-
viduals earlier, we have the best chance of reversing
the effects and improving their quality of life much sooner,”

"BRACAnalysis CDx is a clear-cut example of our commitment to provide high-quality

genetic testing and molecular diagnostics that enable personalized medicine

and improve health outcomes for patients,” says Lloyd Sanders, president of Myriad

Oncology. Pictured here is a lab worker at
Myriad Genetics.
MYRIAD

CONTINUED FROM PAGE 30

chemotherapy. The study results, which were published in the New England Journal of Medicine, indicated that Lynparza maintenance therapy cut risk of disease progression or death by 70 percent.

“SOLO-1 demonstrated the ability of the BRACAnalysis CDx test to accurately identify patients with newly diagnosed, advanced-stage BRCA-mutated ovarian cancer who benefit from Lynparza,” said Dr. Johnathan Lancaster, the chief medical officer of Myriad Genetics. “Importantly, the study findings strongly reinforce the critical importance of BRACAnalysis CDx testing at the time of diagnosis for all patients with ovarian cancer.”

Lynparza is an oral PARP inhibitor being developed by AstraZeneca and Merck & Co. Collaboration between Myriad and AstraZeneca regarding olaparib goes back to 2007 and has resulted in multiple companion diagnostic approvals before the most recent one in newly diagnosed, advanced-stage, BRCA-mutated ovarian cancer.

“We believe this commercial collaboration is another strong indication of Myriad’s global leadership in the field of companion diagnostics for PARP inhibitors and personalized medicine.”

Lloyd Sanders, president of Myriad Oncology

regulatory approvals for BRACAnalysis CDx, as follows:

- Dec. 2014: FDA approved BRACAnalysis CDx as a companion diagnostic to identify patients with advanced ovarian cancer who are eligible for fourth-line treatment with olaparib.
- August 2017: FDA approved BRACAnalysis CDx as a complementary diagnostic to identify patients with ovarian cancer who are eligible for second-line treatment with olaparib.
- January 2018: FDA approved BRACAnalysis CDx as a companion diagnostic to identify patients with metastatic breast cancer who are eligible for second-line treatment with olaparib.
- March 2018: The Japanese Ministry of Health, Labour, and Welfare approved BRACAnalysis CDx as a companion diagnostic to identify patients with metastatic breast cancer who are eligible for second-line treatment with olaparib.

“We congratulate AstraZeneca and Merck on the successful completion and publication of the SOLO-1 trial. These outstanding findings represent another meaningful advancement for patients with ovarian cancer,” said Lloyd Sanders, president of Myriad Oncology.

“BRACAnalysis CDx is a clear-cut example of our commitment to provide high-quality genetic testing and molecular diagnostics that enable personalized medicine and improve health outcomes for patients.”

Less than a week before that news, Myriad announced that the FDA had approved BRACAnalysis CDx to be used by healthcare professionals to identify patients with HER2-negative metastatic breast cancer (mBC) who have a germline BRCA mutation and are eligible for treatment with Pfizer Inc.’s PARP (poly ADP ribose polymerase) inhibitor, Talzenna (talazoparib).

Talzenna is indicated for the treatment of adult patients with deleterious or suspected deleterious germline (inherited) BRCA-mutated HER2-negative locally advanced or mBC. In early October, before the approval had even come through, Myriad had also announced the signing of a commercialization plan with Pfizer in this indication.

“We believe this commercial collaboration is another strong indication of Myriad’s global leadership in the field of companion diagnostics for PARP inhibitors and personalized medicine,” said Sanders at that time. “We are excited to be working with Pfizer and towards ensuring patients have access to this class of drugs.”

After the FDA approval was announced, he added: “We congratulate Pfizer on obtaining FDA approval of Talzenna for certain patients living with metastatic breast cancer, and we are excited to expand the use of BRACAnalysis CDx as the companion diagnostic test. We estimate there are more than 60,000 patients diagnosed with or who progress to metastatic breast cancer in the United States every year who qualify for a BRACAnalysis CDx test.”

The FDA approval was based on results from the EMBRACA trial that evaluated Talzenna vs. physician’s choice chemotherapy in patients with germline BRCA-mutated, HER2-negative locally advanced or mBC.

“Myriad’s BRACAnalysis CDx test was shown in the EMBRACA trial to accurately identify certain patients with a germline BRCA-mutation who may benefit from Talzenna,” said Lancaster. “It is important for patients to know their BRACAnalysis CDx results so they can fully understand their treatment options.”

GENETIC

CONTINUED FROM PAGE 30

said Eileen Braun, executive director of the Angelman Syndrome Foundation.

“Having a cost-effective test to accurately diagnose these syndromes in the newborn period is key to ensuring that families receive optimal medical care and support,” added Theresa Strong, director of research programs for the Foundation for Prader-Willi Research. “The study will validate the newborn screening tool so that, once approved for use, it can be used to screen all babies in the newborn period.”

The study was inspired by Godlee’s previous work to develop a test called MS-QMA, which can accurately diagnose fragile X syndrome, a common genetic disorder linked to autism spectrum disorder. With additional funding, he found the test could also be used to screen for the other three syndromes.

For more information, visit www/DDN-News.com

DIAGNOSTICS

ThyGenX and ThyraMIR data show positive results

Interpace Diagnostics presents favorable new study findings at the 88th Annual Meeting of the American Thyroid Association

BY DDNEWS STAFF

PARSIPPANY, N.J.—In mid-October, Interpace Diagnostics Group Inc. presented new data at the 88th Annual Meeting of the American Thyroid Association (ATA) that support its molecular tests for thyroid cancer. The new interim data, spanning over 300 samples from a two-year “real world” retrospective study, highlighted the clinical utility of Interpace’s ThyGenX thyroid oncogene panel in combination with its micro-RNA classifier, ThyraMIR.

Nine centers across the United States participated in this study, and the data reportedly demonstrated that ThyGenX/ThyraMIR combination test results help avoid unnecessary surgical resections and identify nodules where surgery is appropriate in cytologically indeterminate thyroid nodules. Importantly, the study presented at the ATA meeting also indicated that surgical decisions made based on the combination test results were appropriately aligned with risk of malignancy over clinical and laboratory evaluation.

Recently, Interpace launched an expanded mutation panel called ThyGeNEXT, which includes additional markers such as TERT, PTEN, ALK and RET, among others. As the company’s Clinical Experience Study progresses, patients tested with ThyGeNEXT will also be included to demonstrate the clinical utility of the latest version of the product.
In pursuit of enabling such diagnoses, a partnership is underway to engineer a new method of diagnosing Alzheimer’s disease, while another method has secured Breakthrough Device designation.

Optos plc, a subsidiary of Nikon Corp., and Amydis Inc. have begun a clinical alliance to develop one of Amydis’ eye tests for retinal diagnosis of AD. The partners will work together to develop the test, with Optos applying its proprietary ultra-widefield technology to unite it with Amydis’ proprietary compounds. Financial details for this agreement were not released.

As noted in an Optos press release, “Research shows that damage to the brain [due to Alzheimer’s disease] starts 15 to 20 years before problems become evident … Early and accurate diagnosis could save up to $7.9 trillion in medical and care costs.”

Amydis’ compounds are engineered to detect amyloid proteins in the retina by binding to specific biomarkers and fluorescing, which makes them visible with Optos’ optomap ultra-widefield retinal imaging devices. While traditional retinal imaging can capture between 10 and 100 degrees of the retina, optomap is capable of capturing 200 degrees, with optomap auto-montage reaching 220 degrees.

Robert Kennedy, CEO of Optos, said, “We are proud of the ongoing use of optomap imaging devices in clinical research to visualize biomarkers in the retina associated with Alzheimer’s disease. This clinical collaboration with Amydis supports Optos’ vision to help physicians diagnose and monitor disease by studying the retina. We are pleased to work with Amydis in this important alliance and the benefit it may bring to patients.”

Further down the pipeline, NeuroDiagnostics LLC recently secured Breakthrough Device designation from the U.S. Food and Drug Administration (FDA) for its DISCERN multiple biomarker test for Alzheimer’s disease. Should DISCERN gain FDA approval, it could be the first approved test that uses multiple biomarkers to identify AD and differentiate it from other dementias, according to a NeuroDiagnostics press release.

As with the Optos and Amydis effort, NeuroDiagnostics is pursuing a test that will enable less-invasive diagnosis earlier in the course of the disease. DISCERN only requires a small skin sample to be performed; the sample is incubated and then expanded to more than a million cells.

“The brain is a critical, unmet need for an accurate and simple test for Alzheimer’s disease,” said Dr. Daniel Alkon, principal investigator in the clinical trials for and co-inventor of DISCERN. “Existing methods to identify Alzheimer’s disease have limited accuracy, are expensive and offers invasive; those tests that require lumbar spinal tap are frequently avoided by many patients. Until now, a significant number of patients with dementia go undiagnosed—or worse, misdiagnosed. Each of the NeuroDiagnostics biomarkers independently has been found to show high sensitivity and specificity—in both detecting and differentiating AD from other dementias—as confirmed by autopsy validation.”

DISCERN utilizes three novel proprietary biomarkers, all of which the company says have been proven to be highly accurate, “with a sensitivity and specificity greater than 95 percent in both detecting AD and differentiating AD from other dementias … The three biomarkers comprise an AD-Index assay, a Morphometric Imaging assay and a PKC Epsilon assay. The test can determine the level of synaptic loss in the brain before the onset of amyloid plaques or tangles and is accurate even in the earliest stages of the onset of AD (i.e., years 1-4).”

With the AD-Index Biomarker, NeuroDiagnostics explains on its website that a “small nano-peptide that induces Erk1 and Erk2 phosphorylation in fibroblasts,” after which “quantitative imaging of the phosphorylated Erk1 and Erk2 is then used to identify and differentiate Alzheimer’s disease (AD) from non-AD dementia (Non-ADD) and age-matched control (AC) specimens.”

For the second biomarker, “the cultured skin specimen is stimulated with an extracellular matrix composed of an array of molecules, forming networks which are dysregulated in AD skin fibroblasts. Networks are rapidly formed for Age-matched control and Non-AD dementia cells, but not for AD cells. The rate and extent of network formation can be quantified and is a highly accurate diagnostic biomarker of AD that corresponds to autopsydemonstrated pathologic hallmarks of AD—amyloid plaques and neurofibrillary tangles.”

As for PKC’s (Protein Kinase C’s), a biomarker primarily expressed in the brain and associated with Alzheimer’s pathophysiology, “PKC-specific antibodies are used with the cultured skin specimen to quantify relative levels of PKC’s and to distinguish AD patients from non-ADD and AC patients. AD patients demonstrate a comparative deficit in PKC’s and a different response to the ab stimulus when compared to AC and non-ADD. These differences were found to correspond closely in the AD patients to the presence of amyloid plaques and neurofibrillary tangles.”
**BRIEFS**

_**Ongoing efforts against Huntington’s disease**_

POMPEA, Italy—IRBM and the CHD Foundation have extended their collaboration focused on pursuing new therapeutic approaches to addressing Huntington’s disease. The two partners have worked together since 2011, looking into mechanistic and translational research in addition to tailored drug discovery solutions on IRBM’s part. The extension includes continued access to IRBM’s compound collection and peptide libraries. No additional financial details were disclosed.

“We are proud to be involved with this world-leading initiative to improve the quality of life of patients fighting against this terrible disease. Together with CHD, we are fully committed to help them; they deserve nothing less than our daily dedication,” Piero Di Lorenzo, president and founder of IRBM, said in a press release.

_BioIVT expands blood product offerings_

WESTBURY, N.Y.—The fourth quarter of 2018 saw BioIVT share news of its acquisition of London-based Clinical Trials Laboratory Services (CTLS), which offers high-quality serum, plasma and blood collection services in addition to full-service processing capabilities. Financial details were not released, but BioIVT noted in a press release that all CTLS employees will be joining BioIVT, and the London headquarters of CTLS will function as the combined company’s primary European site for donor collections.

“We are delighted that CTLS is now part of BioIVT,” said BioIVT CEO Jeff Gut. “This is BioIVT’s first donor center in Europe, and we are excited to be able to address our clients’ needs by offering fresh blood and blood-derived products. CTLS expands our immune cell offering, which is one of the fastest growing segments of our company. This acquisition increases our capabilities and improves the efficiency with which we can deliver high-quality biospecimens to our clients in Europe.”

**IN THIS SECTION**

_Awards and honors_

Diamond Pharma named best specialist CRO (Ongoing efforts against Huntington’s disease) 33

_Biomarker discovery/Imaging_ (Ongoing efforts against Huntington’s disease) 33

_Clinical trials_ (Ongoing efforts against Huntington’s disease) 33

_Neurology_ (Ongoing efforts against Huntington’s disease) 33

_M&A activity_ (Ongoing efforts against Huntington’s disease) 33

.Contract services_ (Ongoing efforts against Huntington’s disease) 33

_Diabetes_ (Ongoing efforts against Huntington’s disease) 33

**CONTRACT SERVICES**

**CROs lead industry-wide shift to modernize trial processes**

Roughly nine of 10 CROs are taking steps to unify clinical operations for better visibility and improved study execution

**By MEL J. YEATES**

PLEASANTON, Calif.—Contract research organizations (CROs) continue to lead the adoption of modern clinical applications to increase operational efficiency, simplify trial collaboration and improve study quality, according to a new global industry survey from Veeva Systems. The “Veeva 2018 Unified Clinical Operations Survey: Annual CRO Report” examines CROs’ progress in unifying clinical operations by gathering the experiences and opinions of global CRO respondents, and it examines the drivers, barriers and benefits of a unified clinical operating model.

The report reveals that CROs lead sponsors in adopting purpose-built clinical applications, particularly in study start-up (33 percent of CROs vs. 17 percent of sponsors) and clinical trial management systems (CTMS) (66 percent vs. 54 percent). This momentum is consistent with organizations’ focus on improving study visibility and execution, the two top drivers among CROs for unifying clinical applications.

There are two factors that drive CROs to adopt purpose-built clinical applications. First, the CRO business is examined on page 34.

**Advancing biomarker discovery and therapeutic development**

Specialized CRO offers high-definition tissue imaging services for pharmaceutical and clinical research

**BY DDNEWS STAFF**

SOUTH SAN FRANCISCO, Calif. & PORTLAND, Ore.—The beginning of November saw Sirona Dx, a company involved in high-complexity genomics and proteomics services, announce the introduction of imaging mass cytometry services on the Fluidigm Hyperion Imaging System to advance biomarker discovery and therapeutic development.

Specifically, Sirona Dx is a specialized contract research organization (CRO) that provides high-quality clinical research services to pharmaceutical and clinical research clients and focuses on offering early access to advanced technologies. With a goal of providing innovative approaches to expand drug discovery pipelines and bring more effective therapies to market, the company decided to add multiplex tissue imaging to its growing technology portfolio.

As part of this effort, and having noted “impressive imaging mass cytometry results from top pharmaceutical companies and leading academic medical centers,” Sirona Dx engaged Dr. Akil Merchant, an assistant professor at the University of Southern California Keck School of Medicine, as a scientific advisor to assess its full potential.

“A comprehensive evaluation of different tissue imaging technologies, imaging mass cytometry was the clear choice. Imaging mass cytometry will enable our clients to resolve complex cellular networks and signaling pathways within tissue micro-environments with unprecedented definition,” said Dr. Nasry Yassa, CEO of Sirona Dx. “The early response from our pharma partners has been extremely positive. Our clients are expressing significant interest in this technology.”

Diamond Pharma named best specialist CRO

_Business award granted at OBN in recognition of expert services in cell and gene therapy_

HARLOW, U.K.—In mid-October, Diamond Pharma Services Ltd., a technical services and regulatory affairs consulting group, received the award for “Best Specialist CRO” at the Oxford Bioscience Network (OBN) Awards, in recognition of the company’s expert services in cell and gene therapy.

The OBN Awards, which are celebrating their 10th anniversary, are among the more prestigious awards given to the United Kingdom’s life-sciences industry, and this year sported a record increase in entry numbers—up 48 percent from last year’s total.

Diamond provides strategic and operational services to the pharmaceutical and biotechnology industry. Within the cell and gene therapy field, Diamond’s services and expertise cover all stages of development, including support for engagement with regulatory authorities, dossier writing, scientific advice meetings, orphan designations, pediatric investigations, clinical trial applications, GMP applications and the coordination and leadership for Marketing Authorization applications within the European Union.

Earlier this year, Diamond announced that it supported Kite Pharma Inc. in securing positive CHMP opinion for its breakthrough CAR-T cancer therapy, Yescarta. The regulatory team within Diamond Pharma Services supported in all European regulatory activities throughout the development, submission and regulatory authority review of the Marketing Authorization Application. Diamond also played an integral part in the European regulatory approval of the first gene therapy product, Glybera, in 2012.
TRIAL CONTINUED FROM PAGE 33

incredibly competitive. CROs look for every advantage they can gain over one another. In a world where many services can be viewed as commodities, technology offers compelling differentiation,” says Jim Reilly, vice president of Vault Clinical at Veeva Systems. “The second factor is operational efficiency. Purpose-built, modern platforms allow CROs to drive a higher degree of operational efficiency, while also supporting the scale of their data and process needs.”

“At Atlantic Research Group (ARG), we rarely contract with smaller biotechs that have their own systems or applications in place. For them, an investment in a CTMS would be a significant undertaking. On the other hand, larger companies running many trials likely benefit from implementing these clinical management systems themselves, knowing that they will need them for years to come. Sometimes they even ask us to use their system rather than ours,” adds Hunter Walker, chief technology officer at ARG.

A third (33 percent) of CROs cite collaboration as a challenge. Unified systems and processes as commodities, technology offers compelling differentiation.”

People & Promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-

CROs look for every advantage they can gain over one another. “In a world where many services can be viewed as commodities, technology offers compelling differentiation,” says Jim Reilly, vice president of Vault Clinical at Veeva Systems. “In a world where many services can be viewed as commodities, technology offers compelling differentiation.”

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer
STAMFORD, Conn.—In late October, Cara Therapeutics—a biopharma focused on developing and commercializing new chemical entities, with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors—announced the appointment of Dr. Joana Goncalves as chief medical officer.

Joana Goncalves, M.D.
Chief Medical Officer

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer

SIRONA CONTINUED FROM PAGE 33

in using imaging mass cytometry to advance their research goals and are pleased to access this new technology through an experienced CRO. Sirona Dx has exciting projects underway and additional requests coming in from top pharmaceutical companies.”

Developed for research use, imaging mass cytometry enables simultaneous imaging of up to 37 protein markers from a single scan of formalin-fixed, paraffin-embedded or fresh tissue sec-

people & promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-

CROs look for every advantage they can gain over one another. “In a world where many services can be viewed as commodities, technology offers compelling differentiation.”

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer
STAMFORD, Conn.—In late October, Cara Therapeutics—a biopharma focused on developing and commercializing new chemical entities, with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors—announced the appointment of Dr. Joana Goncalves as chief medical officer.

Joana Goncalves, M.D.
Chief Medical Officer

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer

SIRONA CONTINUED FROM PAGE 33

in using imaging mass cytometry to advance their research goals and are pleased to access this new technology through an experienced CRO. Sirona Dx has exciting projects underway and additional requests coming in from top pharmaceutical companies.”

Developed for research use, imaging mass cytometry enables simultaneous imaging of up to 37 protein markers from a single scan of formalin-fixed, paraffin-embedded or fresh tissue sec-

people & promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-

CROs look for every advantage they can gain over one another. “In a world where many services can be viewed as commodities, technology offers compelling differentiation.”

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer
STAMFORD, Conn.—In late October, Cara Therapeutics—a biopharma focused on developing and commercializing new chemical entities, with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors—announced the appointment of Dr. Joana Goncalves as chief medical officer.

Joana Goncalves, M.D.
Chief Medical Officer

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer

SIRONA CONTINUED FROM PAGE 33

in using imaging mass cytometry to advance their research goals and are pleased to access this new technology through an experienced CRO. Sirona Dx has exciting projects underway and additional requests coming in from top pharmaceutical companies.”

Developed for research use, imaging mass cytometry enables simultaneous imaging of up to 37 protein markers from a single scan of formalin-fixed, paraffin-embedded or fresh tissue sec-

people & promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-

CROs look for every advantage they can gain over one another. “In a world where many services can be viewed as commodities, technology offers compelling differentiation.”

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer
STAMFORD, Conn.—In late October, Cara Therapeutics—a biopharma focused on developing and commercializing new chemical entities, with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors—announced the appointment of Dr. Joana Goncalves as chief medical officer.

Joana Goncalves, M.D.
Chief Medical Officer

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer

SIRONA CONTINUED FROM PAGE 33

in using imaging mass cytometry to advance their research goals and are pleased to access this new technology through an experienced CRO. Sirona Dx has exciting projects underway and additional requests coming in from top pharmaceutical companies.”

Developed for research use, imaging mass cytometry enables simultaneous imaging of up to 37 protein markers from a single scan of formalin-fixed, paraffin-embedded or fresh tissue sec-

people & promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-

CROs look for every advantage they can gain over one another. “In a world where many services can be viewed as commodities, technology offers compelling differentiation.”

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer
STAMFORD, Conn.—In late October, Cara Therapeutics—a biopharma focused on developing and commercializing new chemical entities, with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors—announced the appointment of Dr. Joana Goncalves as chief medical officer.

Joana Goncalves, M.D.
Chief Medical Officer

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer

SIRONA CONTINUED FROM PAGE 33

in using imaging mass cytometry to advance their research goals and are pleased to access this new technology through an experienced CRO. Sirona Dx has exciting projects underway and additional requests coming in from top pharmaceutical companies.”

Developed for research use, imaging mass cytometry enables simultaneous imaging of up to 37 protein markers from a single scan of formalin-fixed, paraffin-embedded or fresh tissue sec-

people & promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-

CROs look for every advantage they can gain over one another. “In a world where many services can be viewed as commodities, technology offers compelling differentiation.”

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer
STAMFORD, Conn.—In late October, Cara Therapeutics—a biopharma focused on developing and commercializing new chemical entities, with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors—announced the appointment of Dr. Joana Goncalves as chief medical officer.

Joana Goncalves, M.D.
Chief Medical Officer

Cara Therapeutics Inc.
Joana Goncalves, M.D.
Chief Medical Officer

SIRONA CONTINUED FROM PAGE 33

in using imaging mass cytometry to advance their research goals and are pleased to access this new technology through an experienced CRO. Sirona Dx has exciting projects underway and additional requests coming in from top pharmaceutical companies.”

Developed for research use, imaging mass cytometry enables simultaneous imaging of up to 37 protein markers from a single scan of formalin-fixed, paraffin-embedded or fresh tissue sec-

people & promotions

HTG Molecular Diagnostics Inc.
Maureen T. Cronin, Ph.D.
Chief Scientific Officer
TUSCUM, Ala.—At the end of October, HTG Molecular, a provider of instruments, reagents and services for molecular profiling applications, appointed Dr. Maureen T. Cronin as the company’s chief scientific officer and senior vice president. Cronin is a veteran biotechnology, translational science and diagnostic executive, bringing to HTG extensive experience in genomic technol-
Partners in immuno-oncology

**MorphoSys and I-Mab sign strategic agreement for novel immuno-oncology agent MOR210**

**BY JEFFREY BOULEY**

PLANEGG, Germany & SHANGHAI—German company MorphoSys AG and Chinese company I-Mab Biopharma recently announced that they have entered into an exclusive strategic collaboration and regional licensing agreement for MOR210, MorphoSys’ proprietary, preclinical-stage antibody directed against C5aR, which has potential to be developed as an immuno-oncology agent.

I-Mab will have exclusive rights to develop and commercialize MOR210 in China, Hong Kong, Macao, Taiwan and South Korea, while MorphoSys will retain rights in the rest of the world. The agreement deepens the existing partnership between the two companies, building upon the ongoing collaboration on MorphoSys’ anti-CD19 antibody MOR202. Under the terms of the agreement, which includes $3.5 million to MorphoSys up front, I-Mab will exercise its exclusive license rights for development and commercialization of MOR210 in its territories. With support from MorphoSys, I-Mab will perform and fund all global development activities for MOR210, including clinical trials in China and the United States, while Tulane University owns perpetual rights to Synagis (palivizumab) in the United States from AstraZeneca for RSV; Tulane awarded NIH contract for whooping cough vaccine.

![Tulane University researchers will put an NIH grant to work on developing a better whooping cough vaccine.](image)

**An acquisition and a contract in infectious disease**

**Sobi to acquire Synagis rights from AstraZeneca for RSV; Tulane awarded NIH contract for whooping cough**

**BY JEFFREY BOULEY**

IN A PAIR OF VERY different developments, but both centered around the issue of infectious disease, Swedish Orphan Biovitrum AB (Sobi) has entered into agreements to acquire the perpetual rights to Synagis (palivizumab) in the United States from AstraZeneca and to participate in 50 percent of the future earnings of the candidate drug MED18897 in the United States, while Tulane University announced that the U.S. National Institutes of Health (NIH) had awarded its school of medicine a contract for up to $8.5 million over five years to develop a more effective and longer-lasting vaccine against pertussis, more commonly known as whooping cough.

Starting with the Sobi and AstraZeneca news, the agreed-upon deal calls for total upfront consideration of $1 billion in cash and $500 million equivalent in newly issued Sobi shares. Synagis is a medicine for the prevention of pertussis, or whooping cough, caused by Bacteroides pertussis; Tulane awarded NIH contract for whooping cough vaccine.

![MorphoSys recently struck a collaboration and licensing deal with I-Mab for MOR210, MorphoSys’ proprietary, preclinical-stage antibody directed against C5aR, which has potential to be developed as an immuno-oncology agent.](image)
INFECTIONOUS

CONTINUED FROM PAGE 35

of serious lower respiratory tract infection (LRTI) caused by respiratory syncytial virus (RSV) infection in high-risk infants—it is the only approved preventative medicine for the condition. Synagis is an attractive product for Sobi due to its orphan patient population and immunology profile. MEDI8897 is a follow-on candidate to Synagis, a monoclonal antibody (mAb) being investigated for the prevention of LRTI caused by RSV in a larger patient population.

“Sobi’s focus on Synagis will enable infants in the U.S. to continue benefiting from this important treatment. Meanwhile, the successful development and commercialization of MEDI8897 remains important for AstraZeneca,” added AstraZeneca’s CEO, Pascal Soriot.

Synagis is an RSV F protein inhibitor mAb that acts as a prophylaxis against serious RSV disease. AstraZeneca has a partnership agreement with AbbVie Inc. for the rights to Synagis outside the United States, which will not be impacted by the proposed transaction.

MEDI8897 is a single-dose, extended half-life anti-RSV F mAb being developed for the prevention of LRTI caused by RSV in all infants entering their first RSV season and children with chronic lung disease or congenital heart disease entering their first and second RSV season. MEDI8897 is being developed for the passive immunization of a broad infant population and has been engineered to have a long half-life so that only one dose will be needed for the entire RSV season. The current development plan includes initiation of a Phase 3 study in healthy full-term and late pre-term infants. MEDI8897 has received Fast Track Designation from the U.S. Food and Drug Administration in March 2015. Moving on to Tulane and the NIH—and away from a virus to a bacterium—microbiologist Dr. Lisa Morici and immunologist Dr. James McLachlan at the university—bacteriologist Dr. Lisa Morici and immunologist Dr. James McLachlan at the university—recognize OMVs secreted by live bacteria during natural infection. They are nanoparticles shed by bacteria that OMVs can do so, and Morici said at the time. “We are particularly excited that we have been selected to present updated preliminary results on all 81 enrolled patients in the L-MIND study, in an oral presentation at ASH. This study is designed to evaluate efficacy and safety of our FC-enhanced CD9 antibody MOR208 in combination with lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma (t/2).”

The release of immune checkpoint blockades within the tumor has become a successful strategy to fight cancers. MOR208 is a novel immuno-oncology asset directed against CgAr by MorphoSys, added Dr. Markus Enzelberger, chief scientific officer of MorphoSys. “By addressing this target molecule, we seek to modulate the tumor microenvironment. We look forward to seeing I-Mab’s investment interest for developing MOR208 program forward into clinical studies, while we retain rights to continue development of MOR202 outside of I-Mab’s territories after clinical proof of concept.”

In addition to the upfront payment, MorphoSys will be eligible for development and commercial milestone payments up to $273 million, as well as tiered, mid-single-digit royalties on net sales of MOR202 in I-Mab’s territories. In addition to partnering with a Chinese company on one of its immuno-oncology candidates, Germany’s MorphoSys also is making progress on two other compounds for blood cancer indications.

Swedish Orphan Biovitrum AB (Sobi) has inked a deal to acquire rights to Synagis, a drug aimed at RSV infection, from AstraZeneca. Based on the U.S. FDA Breakthrough Therapy designation received last year, we are committed to developing MOR208 plus lenalidomide as a new treatment option for patients with t(14;18) DLBCL, where there is a particularly high unmet medical need.”

Specifically, the planned presentations cover:

• MOR208: Results from Phase 1/2a trial of MOR208 plus low-dose dexamethasone (dex) or pomalidomide/dex or lenalidomide/dex in relapsed/refractory DLBCL accepted for oral presentation.

• MOR208 (COSMOS): First data from exploratory Phase 2 COSMOS study of MOR208 plus venetoclax in relapsed/refractory DLBCL accepted for oral presentation.

• MOR202: Results from Phase 12 trial of MOR202 plus low-dose dex or pomalidomide/dex or lenalidomide/dex in relapsed/refractory multiple myeloma accepted for oral presentation.

MorphoSys is a clinical-stage biopharmaceutical company “dedicated to the discovery, development and commercialization of exceptional, innovative therapeutics for patients suffering from serious diseases,” and its focus is on cancer, with investigational therapeutic programs based on its leading expertise in antibody, protein and peptide technologies.

“The year’s ASH meeting will present new updates on our investigational compounds in various blood cancer indications,” Dr. Malte Peters, chief development officer of MorphoSys, said at the time. “We are particularly excited that we have been selected to present updated preliminary results on all 81 enrolled patients in the L-MIND study, in an oral presentation at ASH. This study is designed to evaluate efficacy and safety of our Fe-enhanced CD9 antibody MOR208 in combination with lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma (t/2).”

We thought that if a real infection can engage all the arms of the immune system, then maybe a facsimile of a bacteria could as well.”

Preliminary studies have shown that OMVs can do so, and Morici has used the technology to develop successful vaccines against other diseases such as melioidosis.

“We have worked with outer membrane vesicles for years. They are an extremely potent adjuvant,” said Morici, an associate professor of microbiology and immunology. “An OMV presents to the immune system similar to an intact bacterium—but it’s non-infectious and non-replicating, so it’s much safer.”

CONTINUED FROM PAGE 35

United States.

“Ther growth initiatives. “This acquisition will increase the diversifies our portfolio in immuno-oncology and will form a powerful platform for growth in rare diseases, “said Sobi President and CEO Guido Oelkers. “We see the advantages of our very close working relationship to the benefit of both companies.”

“The release of immune checkpoint blockades within the tumor has become a successful strategy to fight cancers. MOR202 is a novel immuno-oncology asset directed against CgAr by MorphoSys,” added Dr. Markus Enzelberger, chief scientific officer of MorphoSys. “By addressing this target molecule, we seek to modulate the tumor microenvironment. We look forward to seeing I-Mab’s investment interest for developing MOR208 program forward into clinical studies, while we retain rights to continue development of MOR202 outside of I-Mab’s territories after clinical proof of concept.”

In addition to the upfront payment, MorphoSys will be eligible for development and commercial milestone payments up to $273 million, as well as tiered, mid-single-digit royalties on net sales of MOR202 in I-Mab’s territories. In addition to partnering with a Chinese company on one of its immuno-oncology candidates, Germany’s MorphoSys also is making progress on two other compounds for blood cancer indications.
an integral role in helping researchers push the frontiers of genomics across an unprecedented breadth of applications, including whole-genome sequencing, NIFT, liquid biopsy, rare and undiagnosed genetic disease and immune oncology. With the innovation radars of Pacific SBS has, we expect Illumina’s SBS technologies to remain the platform of choice for the majority of sequencing applications moving forward, as our combination of scalability, accuracy and affordability will remain unmatched.”

Illumina leads the market in sequencing solutions, and this deal will bolster its offerings by adding PacBio’s long-read sequencing offerings. Illumina offers short-read sequencing, which will continue to complement its long-read sequencing needs, and with long-read solutions as well, the company will also be able to support customers in applications in de-novo sequencing and sequencing of highly homologous regions of genomes, Illumina reports.

“Accurate long reads can range across longer portions of a genome, helping to resolve ambiguity in assembly, and thereby providing a more comprehensive view of these critical areas of variant,” deSouza explained in a conference call regarding the deal. “For that reason, accurate long-reads have been adopted for applications where access to complex regions is more important than cost or scalability, for example in de-novo assembly and pharmacogenomics. Historically, the challenge for long-read technologies has been accuracy and cost. However, Pacific Biosciences’ recent technology breakthroughs have demonstrated an unparalleled level of accuracy for native long reads, which—when coupled by the impending release of the company’s 8M Smart Cell—will substantially improve the utility and affordability of this technology,” says Francis deSouza, president and CEO of Illumina. “These innovations drive our enthusiasm for bringing our companies’ technologies together now.”

“In Illumina we continue to democratize the use of sequencing at an unprecedented rate. Through this combination, thousands of researchers will now have direct access to this technology,” remarked Dr. Michael Hunkapiller, CEO of Pacific Biosciences. “In Illumina and Pacific Biosciences have shared values and a commitment to innovation. Our complementary sequencing technology, once integrated, will lead toward the development of a new standard of insight and understanding, opening new frontiers of genomic utility.”

“I am extremely proud of the work the PacBio team has accomplished as a standalone company, and I believe that—as part of Illumina—we can continue to innovate our SMRT Sequencing capabilities and reach more customers and address more applications substantially faster than we could do as a standalone enterprise,” he added in the company’s conference call.

The industry seems to mirror that optimism on the whole. Stocks rose 5 percent on news of the agreement. Pacific BioScience Research noted that it was “upbeat” about the deal. Money Tree’s Jim Crumly noted that potential of the deal depended on upcoming advancements from Pacific Biosciences, saying, “The potential for Illumina will be if PacBio can bring the cost of operating its sequencers down to a threshold that opens up major new markets, and company executives believe they are close to that point. Pacifica will be testing a new chip early next year that has 8 million zero-mode waveguides, eight times the number of its current Sequel System.

“The company believes a new model of Sequel with the chip, which could launch in the second quarter of 2019, will put the cost of sequencing the human genome in the ballpark of Illumina’s SBS product, at $1,000 per genome, or one-seventh of what Sequel costs today. Hitting that pivotal price point would open up markets for Sequel where the capabilities of the technology would bring important advantages, but where costs have been a barrier up to now.”

PacBio has continued to push its 4D bioprinting platform to two systems based on the same core technology: NGB-R, a bioprinter marketed currently for research in bio-ink, bio-manufacturing, and NGB-C, a clinical version intended to meet the future needs of Advanced Therapy Medicinal Products production and the requirements of Poietis’ partner.

“We have upgraded the NGB platform to an automated robotic system to improve the standardization of the manufacturing process and the functionality of biological tissues,” said Fabien Guillenot, president and chief scientific officer of Poietis.

**ImmuNoPrism Immune Profiling Kit analyzes tumor composition**

SAN FRANCISCO—Cofactor Genomics has created an RNA-based immune profiling kit for laboratories wishing to derive the immune characteristics of tumor samples. The launch of the kit follows ImmunoPrism announcements on collaborations with The Fred Hutchinson Cancer Research Center and the National Cancer Institute, and the clinical accreditation of the assay by the College of American Pathologists.

“The recent advancements in immunotherapies have resulted in more than 500 drug and combination clinical trials—significantly more trials than there are patients to fill them. Improved tools are needed to provide immune profiling of our tumors, with the goal to ultimately match the right patients with the right trials,” said Dr. Scott Kopetz of both the National Cancer Institute and the College of American Pathologists.

**AMSBIO expands FFPE tissue solutions**

A local company, AMSBio, has expanded its tissue solutions for immunohistochemistry, in-situ hybridization and next-generation sequencing applications. The company has acquired tissue sample quality and experimental setup can lead to misleading results without reliable controls. Traditional cell or tissue-based control specimens often present intra specimen variation, lot-to-lot variations and inconsistent biomolecule quality, driving a need for higher quality controls. CellMax FFPE cell line products are said to be affordable and consistent controls manufactured using a patent-pending process that maintains cell morphology and preserves nucleic acids and proteins. Cells are harvested by using a unique extraction method, preserving cell surface antigens and inflicting minimal physical damage that could lead to a loss of biomarkers. CellMax FFPE cell lines from major cancer types, controls are available in a variety of formats, including whole blocks, arrays and scrolls that can be tailored to suit workflows. These cell line controls exhibit highly consistent density and homogeneity across the entire cell pellet slide and throughout a whole block, allowing accurate results time after time.

A new next-generation electronic batch record execution platform

BASEL, Switzerland—Lonza recently unveiled its next-generation electronic batch record execution platform, as an extension for MODA ES Software Platform. The new platform offers a flexible and cost-effective solution for consolidating and managing batch and quality data produced across cell and gene therapy manufacturing processes.

**The MODA ES Software Platform** has been designed to consolidate, manufacturing batch data, as well as batch-related quality control data, into a single record with an integrated electronic approval interface for expedited product release. With data integrity and traceability at its core, the software reportably captures key quality and performance metrics, while eliminating errors associated with manual and paper-based approaches. Lonza says the platform is flexible, easy to configure and scalable from clinical through to commercial production.

“The MODA ES Electronic Batch Record Execution Platform brings to cell and gene therapy manufacturers the flexibility and informatics tools they desire to scale their processes without compromising safety or compliance,” said Mike Goether, general manager of informatics at Lonza Pharma & Biotech—Biosolutions.

Poiets launches 4D Bioprinting solutions

PESSAC, France—In late October, Poiets introduced one of its NGB bioprinters at the International Congress on Biofabrication in Würzburg, Poietis says they want to establish a new standard in living tissue manufacturing by enabling users, researchers and clinicians to design and bioprint tissues with cellular resolution, and provide new bioprinting solutions covering all needs from research in biology and bioengineering to the production of clinical batches.

Largely inspired by the principles of the 4.0 Industry, the NGB 4D platform is an example of an industrial revolution—these are quantitative measures of specific immune cells in the sampled tumor microenvironment derived from Cofactor’s database of reference immune expression models,” said Dr. Jarrett Glasscock, founder and CEO, a
LONDON & NEW YORK—Cancer Research UK, the Francis Crick Institute and Bristol-Myers Squibb Co. have decided to form a collaboration under which they will create a “rule book” to guide precision combination immunotherapies and to speed up the development of new lung cancer treatments. This new £2.4 million research project will be called RUBICON—which is more or less an acronym for “rule book and immune atlas for combination therapy”—and it will map out the immunology of lung cancer in detail.

The study will be led by Cancer Research UK chief clinician and Francis Crick Institute group leader Prof. Charles Swanton, who said: “Biological therapies, including immunotherapies, are set to transform the way we treat patients, and the RUBICON study will bring us a step closer to this vision.”

“When we see patients with hard-to-treat cancers like lung, we struggle to keep up with the speed at which tumors evolve, become aggressive and resistant to treatment. Our research so far has uncovered many of cancer’s evolutionary secrets, opening opportunities for us to develop new and targeted biological therapies, and understand how they can be combined to maximum effect,” he added. “By learning more about immune suppressive cell types—the molecules they express and how stable they are during disease evolution—we hope researchers can start to develop molecularly targeted immunotherapy combination strategies.”

The project builds on Cancer Research UK’s strategic investment in lung cancer, enhancing its understanding of cancer evolution through tumor samples and data prospectively gathered and analyzed as part of the TRACERx and PEACE studies that were led by Swanton and his team at the Cancer Research UK-Lung Cancer Centre of Excellence at University College London.

Multidisciplinary researchers at the Francis Crick Institute will use state-of-the-art technologies, including deep learning and artificial intelligence tools, to analyze tumor samples and data from TRACERx and PEACE. This will facilitate them in mapping out an atlas of immune cell activity across distinct tumor regions, and in understanding how the incredibly complex tumor immune microenvironment evolves and develops over time.

For its part, Bristol-Myers Squibb will provide £2.4 million in funding for the RUBICON project. “This project is a fantastic example of the industry and charitable sectors working together to support world-class discovery science for the benefit of patients,” noted Veronique Birault, head of translation at the Francis Crick Institute. “The project wouldn’t be possible without Cancer Research UK’s significant investment in research, exemplified by the complementary expertise of three different cancer labs collaborating at the Crick. This new funding will allow our scientists to map out the immune landscape around lung tumors to develop better combination therapies for patients.”

“Bristol-Myers Squibb is proud to be part of this innovative research initiative. We look for first-class science anywhere, and we know that continued progress in cancer can only happen through strong collaboration with scientists, academic researchers, clinicians and patients who participated in clinical trials,” said Dr. Tom Lynch, executive vice president and chief scientific officer of the company. “The U.K. has a strong heritage in cutting-edge research and, through this RUBICON project, we believe further progress will be made for lung cancer patients across the world.”

More evidence for Epidiolex in Dravet syndrome

LONDON—Late November saw cannabinoid-focused biopharma GW Pharmaceuticals plc announce positive top-line results from the second randomised, double-blind, placebo-controlled Phase 3 clinical trial of Epidiolex (cannabidiol or CBD) CV in the treatment of seizures associated with Dravet syndrome, a rare and severe form of childhood-onset epilepsy.

In this trial, Epidiolex, when added to the patient’s current treatment, achieved the primary endpoint of reduction in convulsive seizures for both dose levels (10 mg/kg per day and 20 mg/kg per day) with high statistical significance compared to placebo. Both Epidiolex doses also demonstrated statistically significant improvements on all key secondary endpoints. “The positive outcome in this second trial of Epidiolex in patients with Dravet syndrome further reinforces the effectiveness of this newly available medicine in this particularly difficult-to-treat, childhood-onset epilepsy,” stated Dr. Ian Miller, director of the Epilepsy and Neuropathology Program at Nicklaus Children’s Hospital in Miami and principal investigator of the trial. “The totality of data from the controlled clinical trials completed for Epidiolex have shown clinically meaningful seizure reductions and a consistent safety and tolerability profile.”

The positive results from this trial follow not only the recent U.S. Food and Drug Administration (FDA) approval of Epidiolex for seizures associated with Dravet syndrome and Lennox-Gastaut Syndrome (LGS) in patients two years and older, but also the Drug Enforcement Agency’s rescheduling of the compound (given that marijuana and other cannabinoids are typically still illegal under federal law in the United States). “These data show an effective dose range in Dravet syndrome that is consistent with our FDA-approved label, and which allows for dosing flexibility to address individual patient needs,” noted Justin Gover, GW’s CEO. “We are proud to have recently launched Epidiolex, the first FDA-approved plant-derived cannabinoid medicine, and are excited about its potential to help the lives of patients and their families.”

“The positive results from this latest Epidiolex clinical trial are very encouraging for those living with intractable seizures caused by LGS and Dravet syndrome, two extremely difficult treatment-resistant forms of epilepsy,” said Philip M. Gattone, president and CEO of the Epilepsy Foundation. “This trial increases the body of scientific evidence to support the only FDA-approved cannabinoid therapy and provides hope to the most vulnerable individuals in our epilepsy community who are trying to gain better seizure control.”

“We are proud to have recently launched Epidiolex, the first FDA-approved plant-derived cannabinoid medicine, and are excited about its potential to help the lives of patients and their families.”

Justin Gover, CEO of GW Pharmaceuticals
IntraBio announces clinical results for
Levy body dementia
OXFORD, U.K.—IntraBio Inc., a late-stage biopharmaceutical company developing novel therapies for common and rare orphan neurodegenerative diseases, recently announced results for its lead compound series (IB1000s) for the treatment of dementia, including positive clinical results from compassionate-use studies in patients with Levy body dementia and fronto-temporal dementia, and from preclinical studies in Alzheimer’s disease.

Recent compassionate-use studies with IB1000s in patients with Levy body dementia and fronto-temporal dementia reportedly demonstrated meaningful improvement in quality of life, cognition, mobility, speech and a disease-modifying effect. Clinical examinations and gait analysis revealed marked improvement in gait and balance, and neuropsychological testing revealed measurable improvement of psychomotor function, alertness and attention.

Additional preclinical in vivo studies (in the Npc1−/− mouse model) investigating the effect of IB1000s on Alzheimer’s disease pathology were highly supportive of the treatment’s effect, demonstrating a statistically significant improvement in two critical biomarkers: microtubule-associated protein 1A/1B-light chain 3-phosphatidylinositol-3-phosphate conjugate (LC3-III) was reduced by 68 percent, and amyloid precursor protein C-terminal fragments (APP-CTF) was reduced by 28 percent.

“While the initial sample size is small, to have such a drug with a long-term excellent safety profile showing promising effects in these intractable diseases is very exciting and an important development,” commented Prof. Antony Galione of the University of Oxford and founding scientist of IntraBio.

Levy body’s disease, Levy body dementia and fronto-temporal dementia together account for an estimated 80 to 90 percent of all dementia cases, affecting more than 50 million people worldwide, and are expected to increase in prevalence over the next decades to affect more than 100 million people in 2050.

IntraBio, with its collaborators, has evaluated the effect of IB1000s in com-

Eyenovia has demonstrated the effectiveness of its latanoprost micro-dose on intraocular pressure lowering, which is the main treatment paradigm for conditions such as glaucoma.

Eyenovia announces Phase 2a clinical results in pemphigus vulgaris
NEW YORK—Eyenovia Inc. recently announced that the full results of its Phase 2a Phase 2a study had been published in the article “Latanoprost with high precision, paper micro-dose delivery for IOP lowering: clinical results of the Phase 2a study of 0.4 µg daily microdose” in the November issue of the peer-reviewed journal Clinical Ophthalmology. This is the first study to demonstrate the effect of Eyenovia’s micro-dose on intraocular pressure (IOP) lowering, which is the main treatment paradigm for conditions such as glaucoma. In the study, subjects successfully self-administered high-precision micro-dose latanoprost 84 percent of the time after limited training. This is an important improvement over the standard-of-care eye dropper which is successfully delivered less than half of the time, as demonstrated by multiple peer-review studies. Additionally, micro-dose, which uses 75 percent less drug and preservative than a standard eye drop, achieved 29 percent IOP lowering from baseline—consistent with the 26 percent effect seen in other studies of conventional eye drop latanoprost.

“In addition to our two previous Phase 2 studies in myopia, we believe that P21 further demonstrates that micro-dosing is well tolerated, easily delivered and therapeutically effective without the waste, discomfort and ocular over dosing associated with legacy eye drop delivery. Eyenovia plans to initiate our second front-of-the-eye Phase 3 program, this one in glaucoma, as well as our MicroPine Phase 3 trial for major back-of-the-eye indication of myopic progressive disease in the first half of 2019,” said Dr. Sean Ianchulev, Eyenovia’s CEO and chief medical officer.

TRACON and I-Mab partner on multiple immunology-omnoco programs
SAN DIEGO—Late November saw two clinical-stage companies—TRACON Pharmaceuticals Inc., which focuses on the development and commercialization of novel targeted therapeutics for cancer, and I-Mab Biopharma, a China-based company exclusively focused on the development of innovative biologics in immunology-ainmunotherapies and autoimmunodiseases—junctly announce the establishment of a series of strategic collaborative partnerships for developing multiple immunology-omnoco programs, including I-Mab’s proprietary CD7 antibody TJD5, a novel immunology-omnoco asset with immuno suppression properties and I-Mab’s broad immunology-omnoco portfolio, as well as several proprietary bispes (BsAbs) under development by I-Mab.

TRACON and I-Mab entered into a cost-sharing product development collaboration whereby TRACON will be responsible for the regulatory and clinical development of TJD5 and up to five of the BsAbs in North America, with the majority of the development effort expected to occur in the U.S. TRACON will bear the costs of early phases of clinical trials and I-Mab will share the costs for more advanced development stages and commercialization.

TRACON will also share the North America rights of any selected BsAbs with I-Mab for each collaborative program, with opt-in rights to license the BsAbs from I-Mab in certain territories.

“TJD5 recovers and values the potential of our innovative assets and strong drug discovery and development capabilities,” said Dr. Jingue Zang, CEO of I-Mab. “Partnering with TRACON is an important part of our new global development strategy to bring innovative biologics to patients worldwide. It further strengthens our presence in North America following the establishment of our U.S. office and is an important step to our growing global partnerships spanning from drug candidates to clinical trials.”

Chi-Med enters into multiple collaborations to evaluate drug combo
LONDON—Hutchison China MediTech Ltd. recently entered into four collabora-
tion agreements to evaluate the safety, tolerability and efficacy of Chi-Med’s surufatinib (HMPL-012 or surutiniib) and frucinib in combination with checkpoint inhibitors. It is an important part of Chi-Med’s strategy to explore the potential synergies of its drug candidates in combination with other anticancer treatments. These four new immuno-
therapy collaborations add to ongoing studies combining savolitinib, Chi-Med’s highly selective c-Met inhibitor, with AstraZeneca plc’s checkpoint inhibitor, durvalumab (Imfinzi). The first steps to develop its vascular endothelial growth factor receptor (VEGFR) inhibitors, surufatinib and frucinib, in combination with various programmed cell death protein-1 (PD-1) monoclonal antibodies begin in the following solid tumor settings:

• A global collaboration to evaluate the combination of surufatinib with toripalimab (JS016), a PD-1 monoclonal antibody being developed by Shanghai Junshi Biosciences Co.

• A collaboration in China to evaluate the combination of surufatinib with HX008, a PD-1 monoclonal antibody being developed by Taisho Hanbang Pharmaceuticals, Inc.; and

• A collaboration in China to evaluate the combination of frucinib with ganoclonum (IB2306), a PD-1 monoclonal antibody being developed by Geno Biopharm Co. Ltd.

“Recent innovations in solid tumor drugs have focused on targeted therapies and immunotherapies which, as mono-
therapies, have both provided improved patient outcomes,” said Christian Hogg, CEO of Chi-Med. “We believe that the future of oncology treatments increasingly lies in combining therapies, utilizing multiple mechanisms of action to confront tumors. Our unique next-generation anti-angiogenesis anti-VEGFR inhibitors, with high selectivity and tolerability, make them ideal candidates for such combina-
tions with immunotherapy agents such as PD-1/L1 monoclonal antibodies to probe and expand the benefits of these therapies to more patients.”

Principia reports positive Phase 2b results in pemphigus vulgaris and initiates Phase 3 in pemphigus vulgaris
SOUTH SAN FRANCISCO, Calif.—Principia Biopharma Inc., a clinical-stage bio-
pharma focused on immunology and oncology, has announced positive topline data in the completed open-label Phase 2b trial of PRN1008 in patients with pemphigus (including both pemphi-
gus vulgaris and pemphigus foliaceus) and the initiation of a Phase 3 trial of PRN1008 in pemphigus. The primary efficacy endpoint of the Phase 2b trial—control of disease activity within four weeks—was achieved by more than half of the patients, and PRN1008 was generally well-tolerated. Based on the results of the Phase 2 trial, Principia has initiated the PEGASUS study, a global, randomized, double-blind, placebo-controlled, pivotal, Phase 3 clinical trial to evaluate the ef fect of PRN1008 on the severity of pemphigus—an autoimmune skin disease in which watery blisters form on the skin.

“Pemphigus is a debilitating disease with high unmet need. We are encour-
aged by the efficacy and safety results from the Phase 2 trial and are initiating the Phase 3 trial based on these results. This is a key milestone for Principia, and the next step toward bringing this novel oral therapy to patients in need,” said Martin Bulder, CEO of Principia.

Monalizumab research published in the journal Cell
MARSEILLE, France—Innate Pharma SA in November announced the publication of data in the journal Cell demonstrating the potential of monalizumab, an anti-NKGA2 antibody, which could extend cancer immunotherapies to natural killer (NK) cell-based treatments. This work—led by Prof. Eric Vivier and the Innate Pharma teams in collaboration with MedImmune, the global biologics research and develop-
ment unit of CSL Behring in Belgium, and other renowned researchers and clinicians—will now be used as a reference for later development of monalizumab.

“With a dual effect on T cells and NK cells, monalizumab paves a new path of broad-spectrum immune checkpoint inhibitors,” said Vivier, chief scientific officer of Innate Pharma, a professor at Aix-Marseille University and lead author of the publication. “We hope monalizumab will soon offer a new therapeutic option to a diverse group of cancer patients based on the simul-
taneous blockade of two complementary inhibitory signals, or the combination of inhibitory signal blockade with the delivery of an activating signal.”

“A D V E R T I S E R ’ S I N D E X”
We found that the improvements in the new PHERAstar FSX outperformed our historic experiences and the other readers in our trial.

Mark Wigglesworth, Director of High-Throughput Screening, AstraZeneca, United Kingdom

Visit us at SLAS in Washington from February, 2nd to 6th!