DIAGNOSTICS

BRIEFS

IDT pairs with Ubiquitome for Ebola test

CORALVILLE, Iowa—Integrated DNA Technologies (IDT) and Auckland, New Zealand-based Ubiquitome have launched a partnership for the development of the Ubiquitome Freedom4Real-Time RT-PCR Ebola Virus Assay for easy use in the field. IDT will leverage its PrimeTime qPCR Assay platform to develop an assay that provides accurate, consistent results in testing for Ebola, and the test will be run on the Freedom4, Ubiquitome's handheld, battery-powered real-time PCR device. The assay will be tested by Battelle in Aberdeen, Md.

"The sensitivity and specificity of our PrimeTime qPCR Assays are well established. We are excited about how effectively we can combine IDT's assay design expertise with Ubiquitome's Freedom4 instrument to provide a field testing service for Ebola virus disease. This test will enable early detection and help control the spread of this devastating disease," said Stephen Gunstream, chief commercial officer of IDT.

Epi proColon secures Chinese commercialization

BERLIN & GERMANTOWN, Md.—As announced by Epigenomics AG and BioChain, the China Food and Drug Administration has approved the Epi proColon diagnostic test for colorectal cancer (CRC) for commercialization in China. A major clinical validation study showed the test capable of detecting 75 percent of all cancer cases at 97.5-percent specificity in the Chinese study. BioChain expected to launch the test within weeks of gaining approval.

"We are extremely pleased to announce the approval of Epi proColon in the important Chinese market. BioChain has been incredibly efficient in driving this approval process in a very short time," said Dr. Thomas Taapken, Epigenomics' CEO and chief financial officer. "We now look forward to working closely with our partner BioChain on the launch of this very important diagnostic tool. We are convinced that our test will help to reduce the mortality and costs of care associated with CRC in China through the early identification of the disease."

IN THIS SECTION

Two deals; one goal

Amarantus expands its reach with acquisition deal and license agreement

BY ZACK ANCHORS

SAN FRANCISCO—Amarantus BioScience Holdings has struck two deals that bring it closer to its goal of spinning off a standalone neurodiagnostic company with a comprehensive portfolio of diagnostic tests for Alzheimer's disease and other degenerative disorders. First, the company has acquired DioGenix, a Geneva-based molecular diagnostics company with a pipeline of diagnostic tests focused on immune-mediated neurological diseases; second, it has signed an option agreement with Georgetown University that could lead to an exclusive license to blood-based biomarkers related to Alzheimer's disease.

Gerald Commissiong, Amarantus president and CEO, tells *DDNews* that the company anticipates that DioGenix's diagnostic test for multiple sclerosis (MS) has the potential to generate significant revenue as Amarantus continues to develop its diagnostic products focused on Alzheimer's. "We were attracted to DioGenix because it is in line with our

CREDIT: AMARANTUS

"We were attracted to DioGenix because it is in line with our focus on neurogenerative disorders, but also because of its potential to generate revenues until the Alzheimer's market transitions from an investigational-stage market to a true commercial market opportunity," says Gerald Commissiong, Amarantus president and CEO, of his company's recent acquisition deal.

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Revolution in immuno-oncology

Intratumoral cancer immunotherapy enhances local delivery and uptake of DNA-based immune-targeting agents.

BY ILENE SCHNEIDER

SAN DIEGO—Based on the results of a study showing therapies targeting the programmed death-1 (PD-1) receptor provide unprecedented rates of durable clinical responses in patients with various cancer types, OncoSec Medical Inc. is collaborating with University of California, Los Angeles (UCLA) researchers and PerkinElmer Inc. to help develop biomarker tests to evaluate a patient's immune response to cancer.

The article in the November 27, 2014 issue of the journal *Nature*, titled "PD-1 blockade induces responses by inhibiting adaptive immune resistance," showed the effectiveness of DNA-based intratumoral cancer immunotherapies that combat adaptive

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"These data make an important contribution to our understanding of PD-1 inhibition," says Dr. Robert Pierce, chief scientific officer at OncoSec. "Importantly, the correlation of low TILs with a lack of response to pembrolizumab drives home the need for new therapies that amplify TIL response in those low-TIL patients."

Massing diagnostic efforts in Massachusetts

Diagnostics For All issues challenge grant for Ebola partnership

BY KELSEY KAUSTINEN

BOSTON—In the past decade, Massachusetts has grown to become a hub for life sciences, with dozens of academic and industry organizations calling the state home. And now, several of those firms are banding together in pursuit of a potential Ebola diagnostic.

The partnership will consist of

CREDIT: MASSACHUSETTS LIFE SCIENCES CENTER

Ebola survivor and UMass Medical School faculty member Dr. Richard Sacra and MLSC President and CEO Susan Windham-Bannister at the announcement of a grant to fund a rapid Ebola diagnostic test.

Diagnostics For All, which will lead the undertaking, as well as Harvard University, the Broad Institute, UMass Medical School, GE Healthcare, Cambridge Consultants, Eiken, BBI Solutions, IMPACT Consultants and WellBody Alliance in Sierra Leone.

The goal of the partnership is to produce a field-robust product for test use in six months, based off of technology that Diagnostics For All has already been developing. Diagnostics For All's test incorporates isothermal nucleic acid amplification on a paper substrate and will combine the biological, mechanical and electronic aspects of a molecular diagnostic into a single disposable device that will require a single finger-stick of blood and then provide a "yes/no" response in 45 minutes.

"[We're] charged with implementing the state's 10-year, $1-billion life-sciences initiative, and this grant was

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First to assess BRCA status

Myriad receives FDA approval on companion diagnostic for Lynparza in ovarian cancer

BY LLOYD DUNLAP

SALT LAKE CITY—Myriad Genetics Inc. has received approval from the U.S. Food and Drug Administration (FDA) for BRACAnalysis CDx to be used as the only companion diagnostic in conjunction with AstraZeneca's drug Lynparza (olaparib). Lynparza is the first poly ADP-ribose polymerase (PARP) inhibitor for patients with germline mutations in BRCA1/2 advanced ovarian cancer who have had three or more lines of chemotherapy. BRACAnalysis CDx is Myriad's first FDA-approved companion diagnostic for use with a novel PARP inhibitor.

"Myriad is excited to offer the first and only FDA-approved companion diagnostic for Lynparza, which we believe opens a new door in personalized medicine and represents a big step forward in tailoring treatment for women with ovarian cancer," said Mark Capone, president of Myriad Genetic Laboratories. "Less than 25 percent of ovarian cancer patients know their germline BRCA status, which is critical for any ovarian cancer patient who may be considered for treatment with Lynparza."

BRACAnalysis CDx is reportedly a highly accurate molecular companion diagnostic test that identifies deleterious or suspected deleterious mutations in the BRCA1 and BRCA2 genes, using DNA obtained from a blood sample. The approval of BRACAnalysis CDx is the culmination of an intensive, multiyear scientific collaboration with AstraZeneca to advance personalized medicine for women with ovarian cancer.

CREDIT: MYRIAD

Myriad's BRACAnalysis CDx is the first and only FDA-approved companion diagnostic for Lynparza.

BRACAnalysis CDx is an *in-vitro* diagnostic device intended for the qualitative detection and classification of variants in the protein coding regions and intron/exon boundaries of the BRCA1 and BRCA2 genes. Single nucleotide variants and small insertions and deletions (indels) are identified by polymerase chain reaction (PCR) and Sanger sequencing. Large deletions and duplications in BRCA1 and BRCA2 are detected using multiplex PCR. Results of the test are used as an aid in identifying ovarian cancer patients with deleterious or suspected deleterious germline BRCA variants eligible for treatment with Lynparza. This assay is for professional use only and is to be performed only at Myriad Genetic Laboratories.

"Myriad has proven its ability to navigate a rigorous FDA regulatory approval process that included a comprehensive review of our DNA sequencing, large rearrangement detection and variant interpretation processes. Patients can be confident their BRACAnalysis CDx test results from Myriad are highly accurate," said Capone. "Our scientific excellence, reputation for high quality and regulatory experience are key reasons why Myriad is fast becoming the partner of choice for many biopharmaceutical companies seeking to co-develop companion diagnostic tests. We hope to expand our collaborations and further diversify our product portfolio."

One example of such expansion is being developed for the European market—a BRACAnalysis using tumor tissue that will be valid for both inherited and so-called sporadic mutations caused by errors in cell division or by environmental damage. Ron Rogers, Myriad's executive vice president of corporate communications, estimates this test may identify up to 44 percent more patients eligible for Lynparza than would be by blood test alone.

Myriad Genetics is actively collaborating with several biopharmaceutical companies to further evaluate BRACAnalysis CDx as an investigational companion diagnostic for use with other PARP inhibitors and chemotherapeutic agents and for use in many other solid tumor types. ■

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immunoresistance of cancer. Research led by Drs. Paul Tumeh and Antoni Ribas at UCLA—along with work conducted by Dr. Robert Pierce (currently chief scientific officer at OncoSec) and his colleagues at Merck Research Labs during his previous tenure as executive director at Merck—shows that the response to anti-PD-1 drugs is dependent on the presence of PD-L1 (PD-1 ligand) and tumor-infiltrating lymphocytes (TILs) in the tumor.

"OncoSec is trying to address the population of patients that doesn't respond to PD-1 alone," explains Punit Dhillon, president and CEO of OncoSec. "In immunotherapy, we need to understand how tumor biology works to go after rational approaches for combination therapies that will increase the response rate for various tumor types."

According to Pierce, the approach represents "a revolution in immuno-oncology." Immunotherapy is not simply directed at a particular tumor type, but the test will determine whether a patient has an immune phenotype that will respond to the therapy.

Dhillon adds, "Building on the pioneering work of Dr. Pierce while at Merck, we have focused the potential of ImmunoPulse therapy with IL-12 to enhance TILs in tumors to treat the larger population of cancer patients who are not responsive to anti-PD1 or other checkpoint inhibitors. We are very excited about the potential implications of a successful combination Phase 2b trial of Merck's pembrolizumab and ImmunoPulse."

OncoSec, a biopharmaceutical company developing investigational intratumoral cancer immunotherapy, offers core technology designed to enhance the local delivery and uptake of DNA IL-12 and other DNA-based immune-targeting agents. OncoSec's proprietary technology platform, ImmunoPulse, prompts the body's immune system to target and destroy both local and metastasized cancer cells. Using electroporation, ImmunoPulse delivers brief electrical pulses of DNA IL-12, which stimulates the patient's immune system to destroy cancer cells. ImmunoPulse is designed to stimulate the body's immune system and enable it to recognize, target and destroy cancerous cells.

Clinical studies of ImmunoPulse have demonstrated an acceptable safety profile and preliminary evidence of antitumor activity in the treatment of various skin cancers, as well as the potential to initiate a systemic immune response without the systemic toxicities associated with other treatments. The company has clinical trials underway for melanoma, head and neck cancer and triple-negative breast cancer.

Tumeh and Ribas at UCLA were doing dermatology research on melanomas in a study of 46 patients with advanced melanoma treated with pembrolizumab. The patients underwent tumor biopsies before and during treatment. According to the study, the presence of PD-L1 in tumors alongside tumor-infiltrating CD8+ lymphocytes—a phenomenon that has been termed "adaptive immune resistance"—is a potential biomarker for predicting response to anti-PD-1 drugs. The researchers say that combining anti-PD-1 drugs such as pembrolizumab with therapies that can induce a type-1 interferon-gamma response should be further investigated.

"These data make an important contribution to our understanding of PD-1 inhibition," according to Pierce. "Importantly, the correlation of low TILs with a lack of response to pembrolizumab drives home the need for new therapies that amplify TIL response in those low-TIL patients. We know that IL-12 drives a type-1 interferon-mediated immune response and augments TIL generation, supporting that the combination of ImmunoPulse IL-12 and PD1 blockade will lead to enhanced responses in melanoma."

PerkinElmer has developed a new multiparametric immunohistochemical analysis platform consisting of its Vectra automated quantitative pathology imaging system and its Opal multiplex tissue staining assays, which together can help scientists perform biomarker research to develop a potentially predictive assay to identify the non-responder population. The company will collaborate with OncoSec and UCLA to help researchers develop biomarker tests to evaluate a patient's immune response to cancer.

"We're excited, because it's taken 100 years to get to this point," Pierce says. "Even if only a subpopulation responds to the therapy, the patients respond for a long time. Now we can use biomarkers to tailor studies that will help to increase the response rate." ■

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made through the funding available through that initiative," says Angus McQuilken, vice president for Marketing and Communications at the Massachusetts Life Sciences Center (MLSC). "That initiative was approved by our legislation and signed into law in June 2008, so we're six years into it. We're awarding funding on a regular basis to support projects like this, along with early-stage companies, work-force development efforts, capital projects … this is part of more than $545 million in investment that the center has made thus far to accelerate growth in our life-sciences sectors in Massachusetts, but also to catalyze innovation."

Under this initiative, the MLSC will provide a $1-million challenge grant for the partnership, with a target for the partnership to raise an additional $4.5 million. Diagnostics For All is in talks with a number of parties to raise that amount, and Marcus Lovell Smith, president and CEO of Diagnostics For All, has said he is also seeking additional funding to support taking the device through to final manufacturing and clinical trials.

The company's technology consists of patterning "channels and assay zones of water-repellant materials into a piece of paper roughly the size of a postage stamp. Biological and chemical assay reagents are then deposited in the wells. When blood, urine, saliva, sweat or other biological samples are applied to the device, the paper wicks the sample through the channels to the assay zones, without external pumps or power. Upon contact, the assay zone quickly changes color and results are then easily read by comparing the color change with a reference scale printed on the device. After use, the device can be easily disposed of by burning," the company website notes.

"Rapid testing at the point of care will make a huge difference for the triage process in West Africa and may well save hundreds of lives in the first month it is available," said Dr. Richard Sacra of the University of Massachusetts Medical School. "In many facilities, where lab testing for Ebola is not available, it requires burdensome specimen transport and diagnostic results are often delayed, sometimes over 24 hours, which this rapid diagnostic technology would avoid."

McQuilken tells *DDNews* that the partnership approached the MLSC about six months ago with regard to initiating this project. Given that "An important part of the center's mission is to catalyze innovation that will improve global health," he says, "this project was a great opportunity to accomplish that goal."

"The life-sciences sectors are so important to our state's economy, but more importantly, they enable Massachusetts to make major contributions to the quality of life for people all around the world," according to Dr. Susan Windham-Bannister, president and CEO of the MLSC. ■

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