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THE ONES TO WATCH

A PHARMA MATTERS REPORT.

A REVIEW OF JULY - SEPTEMBER 2011. PUBLISHED NOVEMBER 2011.

Expert review from Thomson Reuters of the most promising drugs changing clinical phase, receiving approval and launched this quarter, based on the strategic data and insight of *Thomson Reuters Pharma*™, the world's leading pharmaceutical competitive intelligence solution.

THE QUEEN'S AWARDS FOR ENTERPRISE: INNOVATION 2008

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The pharmaceutical industry, like many others, faces great challenges in the current economic downturn. In these straitened times, governments, payers, prescribers and patients increasingly want to know the value of new drug products in the real world, and all want to pay for outcomes, not just pills.

The challenge for the industry is not only to develop novel medicines to conquer unmet medical need, but also to develop and articulate strong value propositions in order to make such medicines available to the patients that can benefit from them.

One example of this is the trend towards targeted personalized therapies that has seen the use of computational biology and genetic technologies in oncology research. The resulting treatments are tailored to the genetic profile of sub-populations in whom they will have the greatest effect and be best tolerated.

This edition of *The Ones to Watch* highlights two such treatments that have been launched this quarter, Xalkori® for ALK-positive non-small-cell lung cancer (NSCLC), and Zelboraf™, for BRAFV600E mutation-positive melanoma.

These agents represent a significant advance in the treatment of cancer in general, and the use of personalized medicines in particular. The continued identification of other mutations could lead to the development of many additional drugs not just in oncology but across a range of diseases. These high-value agents are expected to achieve multimillion dollar global sales.

But there is still room for niche markets as the progress of two programs in development for orphan diseases, Swedish Orphan Biovitrum's Kiobrina® and NovImmune's NI-0801, show.

Conversely, other programs in this issue such as Amylin and Lilly's Bydureon™ and Takeda's TAK-875 demonstrate how opportunities also remain in highly established areas like diabetes, where reduced dosing frequency or the opening up of new patient groups can address previously unmet needs.

Let's take a closer look at the five most promising drugs launched or receiving approval, and moving through each of the clinical phases, between July and September 2011.

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THE FIVE MOST PROMISING DRUGS LAUNCHED OR RECEIVING APPROVAL

DRUG	DISEASE	COMPANY
Zoely™	Female contraception	Teva Pharmaceutical Industries/Merck & Co
Bydureon™	Type 2 diabetes	Amylin Pharmaceuticals/Eli Lilly & Co
Xalkori®	Non-small-cell lung cancer	Pfizer
Zelboraf™	Melanoma	Plexxikon/F Hoffmann-La Roche
Horizant™	Restless legs syndrome	XenoPort/ GlaxoSmithKline

Approximately 100 million women worldwide use an oral combined pill as a method of contraception and first in this edition of *The Ones to Watch* we have **Zoely™**, a new contraceptive option developed by Teva Pharmaceutical Industries and licensee Merck & Co.

Teva gained rights to the drug through its January 2011 acquisition of Theramex, a company focused on women's health.

Zoely™ received European approval in August 2011 and launch there is expected by the end of the year; a US filing has also been accepted for review. The product offers for the first time a combined pill containing nomegestrol acetate and the endogenous human estrogen 17β-estradiol. The pill also has a convenient 24-day active and 4-day placebo regimen.

In phase III trials the contraceptive had a lower Pearl Index and a better vaginal bleeding profile than Bayer's Yasmin®, a contraceptive pill which was reported to have the largest share of the market at 33 percent in 2010. *Thomson Reuters Forecast*™ estimates sales of Zoely™ will reach $13 million in 2011 and up to $144 million in 2016, gaining 3 percent of this multi-billion dollar market.

Next up is Amylin and Eli Lilly's once-weekly formulation of exenatide. **Bydureon™** was launched in the UK in July 2011 for the treatment of adults with type 2 diabetes in combination with metformin. Additionally, a PDUFA date has been set by the FDA for January 28, 2012.

The exenatide formulation is delivered using Medisorb®, a biodegradable microsphere technology developed by Alkermes, which allows a continuous release of exenatide via a weekly dose. A pen device is currently being developed by Amylin and Eli Lilly to allow even greater convenience in administration.

In a phase IIIb trial, Bydureon™ was superior to twice-a-day exenatide in reducing HbA1c, and patients in the Bydureon™ arm also lost more weight. In further studies the drug was found to be safe and well tolerated with fewer adverse events compared to competitor products.

Type 2 diabetes is a widespread disease estimated by the World Health Organization (WHO) to affect around 311 million people worldwide. This large market creates high potential for a new treatment option that is safe and requires less frequent dosing, which could result in greater patient compliance. As the first once-weekly treatment for type 2 diabetes to hit the market and with a *Thomson Reuters Forecast* of $2.4 billion in global sales by 2016, Bydureon™ is set to be a blockbuster product, overtaking the once-a-day exenatide formulation.

Our next treatment to hit the market is **Xalkori®** (crizotinib), a first-in-class oral ATP-competitive dual inhibitor of c-Met (hepatocyte growth factor receptor tyrosine kinase) and ALK (anaplastic lymphoma kinase). The drug is indicated for the treatment of ALK-positive, advanced NSCLC.

Alterations in the ALK gene are thought to be a key driver of tumor development in cancers such as NSCLC and studies suggest 3 to 5 percent of NSCLC patients have tumors positive for mutant ALK. Xalkori® blocks signaling in several cell pathways that are critical for the growth and survival of tumor cells. Xalkori® has been approved in parallel with a companion diagnostic test developed by Abbott Molecular. The test, known as the Vysis ALK Break Apart FISH Probe test, can determine if a patient's tumor shows chromosomal rearrangements involving ALK, allowing therapy tailored to the tumor's genotype.

Lung cancer is reported to be the cause of more deaths worldwide each year than any other type of cancer, and NSCLC accounts for 85 percent of these cases. Xalkori® is the first therapy to be approved specifically for this NSCLC patient sub-population and is also the first ALK inhibitor to reach the market. With a promising disease control rate of 80 percent in phase II trials, the drug is expected to prove a major advance in this largely unmet medical need.

FDA approval was received in August 2011 and the drug was made immediately available through a number of specialty pharmacies; approval is pending in Europe. *Thomson Reuters Forecast* predicts global sales of $657 million in 2015.

Our next newly approved drug is also a personalized treatment for cancer, this time targeting BRAFV600E mutation-positive melanoma. **Zelboraf™** (vemurafenib) is the first personalized treatment to be approved in the US for this population of metastatic melanoma patients.

Metastatic melanoma is the deadliest and most aggressive form of skin cancer affecting an estimated 10,000 people worldwide each year with around half of patients positive for the BRAFV600E mutation. Zelboraf™ targets and blocks the mutated B-RAF protein inside cells. In a phase III trial it improved overall survival, and significantly reduced the risk of death and the risk of disease progression by 63 and 74 percent, respectively, compared to dacarbazine.

Although the target market is limited due to the specificity of the treatment, Zelboraf™ is still expected to command global sales of $649 million in 2016, according to *Thomson Reuters Forecast*.

Zelboraf™ was developed by Plexxikon and F Hoffmann-La Roche, a subsidiary of Roche Holding, and is also intended to be used in conjunction with a diagnostic test, COBAS 4800 B-RAF V600, which was developed by Plexxikon in collaboration with Roche Molecular Systems. The drug and the test are to be co-promoted in the US by Daiichi Sankyo, which acquired Plexxikon in April 2011, and Genentech, a US subsidiary of Roche.

Our final drug in this section is **Horizant™**, a once-daily tablet formulation of the GABA modulator, gabapentin enacarbil. Launched in the US in July 2011, the drug was developed by GlaxoSmithKline and XenoPort for the treatment of restless legs syndrome (RLS).

RLS is a neurological disorder which can have a debilitating effect on daily life. Around 2 to 3 percent of adults worldwide are thought to be affected by moderate-to-severe RLS, with a further 5 percent affected by a milder form. The disorder is usually treated with dopaminergic agents such as Mirapex® (pramipexole) or ReQuip® (ropinirole). However, these medications can cause nausea and dizziness, worsening of symptoms following long-term use, and development of impulsive or obsessive behaviors.

Horizant™ is the first non-dopaminergic therapy to be approved and marketed for RLS. Upon ingestion, Horizant™ is converted into gabapentin which binds to a specific calcium channel with no affinity for other common receptors. In a phase III study, Horizant™ significantly improved symptoms of RLS with 78 percent of patients 'much improved' or 'very much improved' according to the CGI-I (Clinical Global Impression-Improvement) scale, compared with 45 percent of placebo-treated subjects.

The drug is forecast to achieve global sales of $363 million in 2016 gaining a 12 percent share of the market currently dominated by Mirapex®.

THE FIVE MOST PROMISING DRUGS ENTERING PHASE III TRIALS

DRUG	DISEASE	COMPANY
VEN-309	Hemorrhoids	Ventrus Biosciences
CF-101	Xerophthalmia	Denali Concrete Management
Kiobrina®	Exocrine pancreatic insufficiency	Swedish Orphan Biovitrum
LAS-40464	Chronic obstructive pulmonary disease	Almirall Prodesfarma/ Forest Laboratories
TAK-875	Diabetes mellitus	Takeda Pharmaceutical

VEN-309 is an ointment formulation of the vasodilator and platelet aggregation inhibitor iferanserin (also known as TJN-219). The drug is under development by Ventrus Biosciences, which licensed the drug from Amer & Co in March 2008, for the treatment of hemorrhoids.

According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), symptomatic hemorrhoids affect around 12.5 million adults in the US but currently there are no prescription drugs approved for treatment by the FDA. Available OTC drugs soothe inflammation by reducing swelling and redness but do not cure the disorder, and can only be used for 5 to 7 days in case they irritate the sensitive skin. Corticosteroids are sometimes prescribed to reduce the inflammation but should also not be used for longer than a week in case they thin the skin.

VEN-309, a 5-HT_{2A} receptor antagonist, works by improving the blood flow out of dilated veins, reducing the symptoms of bleeding, itchiness and pain. A phase III trial of the drug was initiated in August 2011 and data are expected in February 2012.

Our second new phase III candidate in this quarter's *The Ones to Watch* is Denali Concrete Management's **CF-101**. In August 2011, a phase III trial was initiated to evaluate a tablet formulation of the adenosine A_3 receptor-targeting, TNFα-suppressing compound for dry eye.

Denali, whose original focus was on providing improved concrete solutions to the road construction industry, may not seem a likely company to be involved in pharmaceuticals . However, having ceased trading due to a challenging business environment, the company sought new opportunities leading in June 2011 to the licensing of CF-101 from Can-Fite Biopharma, which is now also a major shareholder in the company. CF-101 is being developed by an Israel-based subsidiary of Denali for ophthalmic indications, including glaucoma and uveitis.

Over 30 million people worldwide, including contact lens users and postmenopausal women, suffer from dry eye syndrome. It also occurs in an autoimmune disease known as Sjögren's syndrome where immune cells destroy the exocrine glands that produce tears and saliva. Current standard of care involves the administration of eye drops multiple times daily to provide lubrication and symptomatic relief, but this does not cure the disease. CF-101 attacks pathogenic cells that express high levels of the adenosine A_3 receptor. On this basis, Can-Fite is also developing the drug for the treatment of autoimmune diseases such as rheumatoid arthritis, osteoarthritis and psoriasis.

The double-blind, randomized, multicenter, 24-week phase III trial for dry eye is being conducted in 240 patients in Israel and is expected to complete in August 2012.

In the US, around half a million infants are born prematurely, accounting for approximately 12 percent of all births each year. Causes of prematurity include multiple births, cervical incompetence, abnormalities in the placenta or uterus, trauma and infection. The rise in premature births, particularly among older women, is associated with the increase in multiple births through assisted reproduction. Because of this increase and the increased proportion of premature infants that survive, there is a greater need for drugs to help support infant growth and development.

Bile-salt-stimulated lipase (BSSL) is a natural constituent of breast milk and is important for fat digestion in preterm infants. Swedish Orphan Biovitrum's **Kiobrina®** (bucelipase alfa) is a recombinant human lipase (rhBSSL) with the same amino acid sequence and properties as natural BSSL. Swedish Orphan believes that adding rhBSSL to pasteurized breast milk or infant formula for preterm infants with pancreatic insufficiency will restore the activity level of natural lipase that is lost during breast milk pasteurization or absent in formula milk, thus improving growth velocity. The drug has been awarded Orphan status in Europe for fat malabsorption in patients with exocrine pancreatic insufficiency.

Phase II data have shown that the addition of Kiobrina® to both formula and breast milk significantly improves growth velocity compared to placebo, with no adverse events reported. A multicenter, European, double-blind, placebo-controlled, phase III study is being conducted in 432 preterm infants younger than 32 weeks of gestational age. The study is expected to complete in August 2013.

Swedish Orphan Biovitrum (previously known as Arexis) licensed the drug from AstraZeneca in February 2004.

The next agent entering phase III is **LAS-40464**, an inhaled combination of the muscarinic M_3 antagonist, Eklira® (aclidinium bromide), and the long-acting β_2 adrenoceptor agonist, Foradil® (formoterol). LAS-40464 is being co-developed by Almirall Prodesfarma and Forest Laboratories for the treatment of chronic obstructive pulmonary disease (COPD).

The WHO estimates that in 2007, 210 million people were affected by COPD, with 3 million patients dying from the disease in 2005. Globally COPD is believed to account for 5 percent of deaths, a figure expected to increase by 30 percent over the next 10 years. Studies have shown 60 percent of COPD patients will report some limitations in their daily activities and an impaired quality of life. Patients will also often demonstrate periodic worsening of symptoms. While new COPD treatments will clearly be of benefit to patients, it is also a lucrative market for pharmaceutical companies. In 2008 and 2009, worldwide sales of Novartis' Foradil® reached $490 million and $455 million, respectively.

Phase II trials of LAS-40464 showed a significant difference in normalized $AUC_{0\text{-}12h}$ FEV1 versus placebo. In addition, improved bronchodilation was observed compared with Eklira® and Foradil® monotherapy. Two phase III trials of the drug are underway in the US and are expected to enroll a total of 2000 COPD patients.

The last drug to make the phase III section this quarter is Takeda's glucose-dependent insulin secretagogue and G protein-coupled receptor-40 (GPR-40) agonist, **TAK-875**, which uses an insulinotropic therapeutic mechanism different to that of sulfonylureas or incretin-like compounds, and is the first selective GPR-40 agonist to reach clinical development for type 2 diabetes. The company initiated three phase III trials of a tablet formulation of TAK-875 in September 2011.

Data from a Japanese phase II study showed 100 or 400 mg of TAK-875 administered over 14 days to 65 type 2 diabetics, rapidly and effectively improved postprandial and fasting hyperglycemia (-45.6 and -33.9 mg/dl in the 400 and 100 mg dose groups, respectively) with a low risk of hypoglycemia.

The EMA has approved a pediatric investigation plan for the drug, potentially increasing its value and market share.

THE FIVE MOST PROMISING DRUGS ENTERING PHASE II TRIALS

DRUG	DISEASE	COMPANY
OTO-104	Ménière's disease	Otonomy
EMA-401	Postherpetic neuralgia	Spinifex Pharmaceuticals
POT-4	Age related macular degeneration	Potentia Pharmaceuticals
NI-0801	Primary biliary cirrhosis	NovImmune
DRL-17822	Hyperlipidemia	Dr Reddy's Laboratories

The first agent entering phase II studies in this edition of *The Ones to Watch* is **OTO-104**, a locally-acting, sustained-release thermosensitive gel formulation of the steroid dexamethasone, delivered via intratympanic injection. OTO-104 is being developed by Otonomy, a biopharmaceutical company focused on developing therapies for middle and inner ear disorders.

In September 2011, a phase II study was initiated in the US to assess the safety and efficacy of the drug in patients with unilateral Ménière's disease, a debilitating disorder of the inner ear that affects balance and hearing and involves symptoms such as vertigo, tinnitus and hearing loss. The exact cause of the disease is unknown and there are no FDA-approved medications, although injection of steroids directly into the ear has been found to ease symptoms in some cases. Hearing and balance disorders such as Ménière's disease affect nearly 30 million Americans, and with no approved treatments there is a high unmet medical need.

OTO-104's thermosensitive gel formulation allows for greater drug exposure time in the middle ear, offering an advantage over aqueous solutions which rapidly drain away via the Eustachian tube. The company believes intratympanic injection treatments could help transform the treatment of hearing and balance disorders in a similar way to intravitreal injections in the field of ophthalmology.

In a phase I study, OTO-104 was well tolerated, with patients who received the drug showing greater reductions in vertigo frequency and tinnitus compared to placebo.

Postherpetic neuralgia (PHN) is a painful condition caused by nerve damage that occurs in some individuals following a herpes zoster infection or shingles as it is more commonly known. While existing therapies work in some PHN patients, a significant number either do not respond to treatment or experience adverse events. Researchers at the University of Queensland made the discovery that angiotensin II type 2 (AT_2) receptor antagonists may offer a novel approach to treating the disease.

Having licensed the University's AT_2 receptor technology, Spinifex Pharmaceuticals, an Australian biotechnology company, is now developing **EMA-401**, the lead from a program of small molecule AT_2 antagonists as a potential first-in-class oral treatment for PHN.

In September 2011, Spinifex dosed the first patients in a phase II proof-of-concept study which is expected to include 170 patients. The primary endpoint is the reduction in mean daily pain score compared with placebo during the last week of a 28-day treatment period.

EMA-401 has previously demonstrated efficacy in pre-clinical studies and has shown good safety and pharmacokinetics in phase I trials. Alongside PHN, Spinifex intends to develop the drug for other neuropathic pain indications which are projected to form a $6.2 billion market by 2017.

The leading cause of blindness in Western countries is age related macular degeneration (AMD) which occurs in two forms: wet and dry. Current treatments are primarily focused on angiogenesis inhibitors and target the wet form of the disease, which accounts for 10 to 15 percent of sufferers. There are no approved drugs on the market for those affected by dry AMD however.

A potential treatment for both dry and wet AMD is Potentia's **POT-4**, a sustained-release intravitreal implant formulation of a derivative of the 13-mer cyclic peptide, compstatin. Potentia licensed the drug from the University of Pennsylvania in August 2006, and in October 2009 entered into a licensing and purchase option agreement with Alcon Research.

POT-4 binds to complement C3, preventing downstream complement activation in all three complement activation pathways, which may otherwise result in inflammation, tissue damage and upregulation of angiogenic factors. It was the first complement inhibitor to enter clinical development for AMD, when a phase I study was initiated in March 2007. In this trial, the drug was safe with no reported cases of drug-related toxicity, serious adverse events or intraocular inflammation.

A phase II study to compare POT-4 plus Genentech's Lucentis® (ranibizumab) with Lucentis® alone in patients with wet AMD was initiated in the US in July 2011 and is expected to be completed in December 2011.

Our next phase II agent of interest is **NI-0801**, a fully human monoclonal antibody which targets human IP-10 (chemokine interferon inducible protein 10), under development by NovImmune for autoimmune and inflammatory diseases.

IP-10 is produced by various cell types during inflammation, recruiting T-cells and natural killer cells to tissues. By blocking the recruitment and activation of pathogenic cells at the site of inflammation, NI-0801 offers a potential treatment for a variety of diseases, including primary biliary cirrhosis (PBC), which is the focus of a current phase II study. The proof-of-concept, open-label trial began in September 2011 in Italy and the UK, and will assess multiple doses of the drug in PBC patients.

PBC is an orphan autoimmune disease that predominantly occurs in middle-aged females. Small bile ducts in the liver, which drain bile into the gallbladder, become inflamed and leak bile acids into the liver tissue. As damage progresses, scarring or cirrhosis occurs which may eventually lead to liver failure and the need for a transplant. Early symptoms of the disease include nausea, tiredness, itching, abdominal pain and jaundice. Currently there is no cure for the disease, only symptomatic treatments, leaving a significant gap for new therapeutic options. NI-0801 has proved safe and well tolerated in two phase I studies conducted in healthy volunteers.

The leading cause of death worldwide in men and women is cardiovascular disease. Coronary artery disease caused by atherosclerosis, a thickening of the arteries, is responsible for greater morbidity and mortality than any other cardiovascular disorder.

Atherosclerosis occurs when substances such as cholesterol build up in the walls of the arteries forming plaques. Statins are widely used to treat elevated lipid levels and work by lowering low-density lipoprotein (LDL) cholesterol. However, a significant cardiovascular risk remains with statin therapy.

An alternative approach is to raise high-density lipoprotein (HDL) cholesterol levels and one way of achieving this is by targeting CETP (cholesteryl ester transfer protein), an approach being investigated by Dr Reddy's Laboratories with the development of **DRL-17822**.

DRL-17822 is a selective, orally active, CETP inhibitor with the potential to treat dyslipidemia, atherosclerosis and associated cardiovascular diseases. Dosing in a European, phase II study to assess the safety and efficacy of the drug in 160 patients with type-II dyslipidemia began in September 2011.

The primary endpoint will be change from baseline in HDL cholesterol and LDL cholesterol compared to placebo. The drug has proved safe and well tolerated in three phase I European studies and proof-of-concept was shown by dose-dependent inhibition of plasma CETP activity, increases in HDL cholesterol, and decreases in LDL cholesterol.

THE FIVE MOST PROMISING DRUGS ENTERING PHASE I TRIALS

DRUG	DISEASE	COMPANY
ACH-2928	Hepatitis C virus infection	Achillion Pharmaceuticals
PU-H71	Cancer	Memorial Sloan-Kettering Cancer Center
PWT-33597	Cancer	Pathway Therapeutics
OPN-305	Inflammatory disease	Opsona Therapeutics
ME-143	Solid tumor	Marshall Edwards

The WHO estimates that worldwide, 170 million people are chronically infected with hepatitis C virus (HCV). Meanwhile the US Centers for Disease Control and Prevention (CDC) suggests that at least 20 cases go unreported for every 1 that is recorded due to long asymptomatic periods in infected individuals, and its high prevalence in populations unlikely to be tested, such as the institutionalized, the homeless and injecting drug users. Although the incidence of new HCV infections is on the decline, the disease burden is rising due to the aging HCV-infected population.

The current standard of care is a 48-week course of peginterferon alfa and ribavirin, but the efficacy of this regimen is varied and dependent on HCV genotype, host genetics, disease severity, age of the patient, and viral load. The regimen is also associated with a variety of side effects that can impact patient compliance.

The NS5A protein of HCV is involved in various stages of the virus's life cycle including virion production, interaction with host proteins and interferon resistance. Achillion Pharmaceuticals initiated a first-in-man, phase I trial of its NS5A protein inhibitor, **ACH-2928**, in July 2011. In pre-clinical studies, the compound demonstrated high potency against HCV RNA replication and showed synergy with both interferon and ribavirin.

ACH-2928 is Achillion's first NS5A protein inhibitor to advance to the clinic and the company has plans to advance a second. Achillion hopes the trial will demonstrate human proof-of-concept.

Heat shock protein (Hsp) 90 is one of the most abundant proteins in a human cell and acts as a molecular chaperone to assist the folding or disassembly of other proteins and also plays a role in cell signaling and tumor suppression. Hsp90 stabilizes a variety of growth factors, including phosphatidylinositol 3-kinase (PI3K) and protein kinase B (also known as Akt) and it is thought that inhibition of the protein induces apoptosis through the PI3K/Akt signaling pathway.

Our second agent entering phase I trials this quarter is Memorial-Sloan Kettering Cancer Center's lead Hsp90 inhibitor, **PU-H71**. The trial, which began in July 2011, is enrolling patients in the US with advanced malignancies, including lymphoma, and is expected to complete in July 2013.

In December 2009, pre-clinical data were presented at the 51st ASH meeting in New Orleans, LA. Mice transplanted with a cancer cell line and treated with PU-H71 were still alive after 28 days while all vehicle-treated mice died within 15 days.

The compound has also demonstrated activity in pre-clinical studies for Alzheimer's disease and multiple sclerosis, diseases both associated with aberrant protein species.

Following on from the PI3K signaling pathway, our next compound to enter phase I this quarter is Pathway Therapeutics' **PWT-33597**, a dual PI3K and mammalian target of rapamycin (mTOR) inhibitor, for cancer. Activation of PI3K activates Akt which, in turn, leads to mTOR activation. In cancer, this signaling pathway is overactive, reducing apoptosis and increasing proliferation. Pre-clinical research has shown that inhibition of both PI3K and mTOR is more effective than inhibiting either target alone.

Initiation of this trial was supported by over $12 million in private funding involving several Australian investment firms and the Breast Cancer Research Trust. The study is enrolling 72 patients in the US with advanced malignancies.

Although there are several other dual inhibitors in various stages of development by other companies, no dual-acting compound has yet reached phase III development. One of the most advanced programs is Novartis' BEZ-235, which has been evaluated in a phase I/II trial for solid tumors and for which a phase II study for endometrial cancer is planned.

Opsona is an Irish company focused on autoimmune and inflammatory diseases which was founded in March 2004 as a spin-off from Trinity College in Dublin, Ireland. In this quarter, the company initiated a phase I trial of **OPN-305**, its IgG4 humanized monoclonal antibody targeting TLR-2 (toll-like receptor 2) for inflammatory diseases, including conditions associated with solid organ transplantation.

Opsona has several funding and manufacturing deals in place for OPN-305. The MABSOT (Monoclonal Antibody Solid Organ Transplantation) consortium comprises several research and clinical groups including King's College and Euram, and has the primary objective of progressing OPN-305 through phase I and IIa trials for the prevention of delayed graft function in renal transplantation. By May 2011, Opsona had received €5.9 million (approximately $8.06 million) in funding from the European Commission to lead the consortium.

The randomized, double-blind, placebo-controlled trial is enrolling healthy subjects to receive a single intravenous dose of the drug. Phase II trials of the drug are expected to begin in 2012.

Marshall Edwards is taking a different approach to the treatment of solid tumors with its NADH oxidase inhibitor, **ME-143** (previously known as NV-143). ME-143 is a metabolite of NV-196, a second-generation derivative of phenoxodiol. The drug was previously being developed by Marshall's parent company, Novogen. In December 2010, following shareholder approvals, the companies entered a definitive asset purchase agreement for Marshall to acquire Novogen's isoflavone-based intellectual property portfolio.

ME-143 is derived from the company's isoflavone technology platform. Pre-clinical studies have so far shown its superiority to phenoxodiol and NV-196. It has also demonstrated superior synergistic activity with platinum-based chemotherapy.

The dose-escalation, open-label trial is enrolling 24 patients with refractory solid tumors and is being conducted in collaboration with the Sarah Cannon Research Institute.

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