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R&D FOCUS
drugnews
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trastuzumab

Roche registered & marketed, USA (gastric cancer)

Roche reported on 21 October 2010 that the US FDA has approved trastuzumab (HERCEPTIN) in combination with cisplatin plus either capecitabine or 5-fluorouracil and cisplatin for the first-line treatment of HER2-positive metastatic cancer of the stomach or gastroesophageal junction. The antibody is now available in the USA for this indication.

Trastuzumab, a humanized monoclonal antibody directed against HER2, is available in the USA, Canada, the EU and several other territories worldwide for the treatment of metastatic breast cancer. The antibody was made available in Canada in August 2010 for gastric cancer. Trastuzumab is approved in the EU for this indication and was launched in the UK in February 2010.

Launches

GLASSIA

Baxter marketed, USA (enzyme deficiency)

GLASSIA has been launched in the USA for chronic augmentation and maintenance therapy in adults with emphysema due to congenital alpha1 antitrypsin deficiency, Baxter announced on 25 October 2010. GLASSIA is an intravenous alpha1 antitrypsin under development by Kamada. Baxter obtained exclusive commercialization rights to the agent in the USA, Australia, New Zealand and Canada in August 2010.

prasugrel

Lilly marketed, India (acute coronary syndrome)

Lilly announced on 26 October 2010 that prasugrel (EFFIENT) has been launched in India. The agent, an oral

R&D Focus Drug News

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See R&D Focus (Drug Updates) for full product details

Contents

antithrombotic prodrug that inhibits the ADP receptor, is indicated for use in patients with acute coronary syndrome who have undergone angioplasty procedures. Prasugrel, which was discovered by Daiichi Sankyo, is available in approximately 70 countries worldwide, including the USA, the EU, Canada, Australia and Argentina.

Approvals

dasatinib

Bristol-Myers Squibb recommended for approval, EU (CML)

Bristol-Myers Squibb announced on 22 October 2010 that the CHMP of the EMA has adopted a positive opinion, recommending the approval of dasatinib (SPRYCEL) for the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (CML) in chronic phase. The recommendation was based on 12-month results from the ongoing phase III DASISION trial in this patient population. An sNDA in this indication is pending approval in the USA.

Dasatinib, an Abl and Src tyrosine kinase inhibitor, is under development for the treatment of CML, acute lymphoblastic leukemia (ALL), multiple myeloma and various solid tumors. Dasatinib has been launched in several major markets worldwide, including the USA, the EU, Canada and Japan for the treatment of CML and ALL patients who are resistant or intolerant to prior therapy.

dexmedetomidine

Orion filing accepted for review, EU (anesthesia general)

Orion announced on 20 October 2010 that the EMA has validated the company's MAA for dexmedetomidine (PRECEDEX), and initiated the review. Orion is seeking approval via the centralized procedure for use of the agent in intensive care sedation.

Dexmedetomidine, an alpha2 adrenergic agonist, was first launched in the USA in March 2000 for continuous iv sedation of intubated and mechanically ventilated patients in the intensive care setting for up to 24 h. The agent has subsequently been launched for the same indication in various other territories worldwide.

BEMA fentanyl

Meda registered, EU (pain)

BioDelivery Sciences International and Meda announced on 20 October 2010 that BEMA fentanyl, a transmucosal fentanyl product, has been approved in Europe via the decentralized procedure, under the trade name BREAKYL, for the management of breakthrough pain in opioid-tolerant, adult cancer patients. Marketing authorizations will follow in the individual countries, expected over the next few months and throughout 2011. Meda submitted the regulatory application for BEMA fentanyl in April 2008, with Germany acting as the Reference Member State. BioDelivery Sciences International is due to receive a US$2.5 million milestone payment from Meda, triggered by the first national marketing authorization in Europe. A second US$2.5 million payment from Meda will be paid at the time of the first commercial sale, expected before the end of 2011. BioDelivery Sciences International will receive a double-digit royalty on net sales.

BEMA fentanyl utilizes BioDelivery Sciences International's Bioerodible Mucoadhesive (BEMA) delivery system, which consists of a thin film incorporating drug that adheres to the oral mucosa and erodes with time, releasing the drug into the tissue. In October 2009, the product was launched in the USA, under the trade name ONSOLIS, for the management of breakthrough pain in adult cancer patients. ONSOLIS has also been approved in Canada for the management of breakthrough cancer pain in adult, opioid-tolerant patients. In August 2006, BioDelivery Sciences International licensed European rights to BEMA fentanyl to Meda. As a result of subsequent licensing agreements between the two companies, Meda has acquired worldwide rights to the product, excluding South Korea and Taiwan.

lorcaserin

Arena Complete Response letter, USA (obesity)

Arena and Eisai announced on 23 October 2010 that they have received a Complete Response letter from the

See R&D Focus (Drug Updates) for full product details

US FDA relating to Arena's NDA for lorcaserin for weight management, including weight loss and maintenance of weight loss, in obese and overweight patients with at least one co-morbid condition. Non-clinical and clinical reasons were cited by the FDA for why it cannot approve the NDA in its current form. Non-clinical issues included diagnostic uncertainty in the classification of mammary masses in female rats, an unresolved exposure-response relationship for lorcaserin-emergent mammary adenocarcinoma, as well as an unidentified mode of action and unclear safety margin for lorcaserin-emergent brain astrocytoma. The Complete Response letter requested additional information to address these issues. The FDA stated that weight loss efficacy in overweight and obese patients who do not have type II diabetes was marginal, and recommended that Arena submits data from the completed BLOOM-DM trial of lorcaserin in overweight and obese patients with type II diabetes. The FDA also indicated that further clinical trials may be required in the event that evidence to alleviate concern relating to tumor findings in rats cannot be provided. Arena intends to request a meeting with the FDA to clarify these requests.

Lorcaserin is an orally administered selective 5-HT2C agonist. Eisai acquired exclusive US rights to lorcaserin from Arena in July 2010.

ranibizumab

Novartis recommended for approval, EU (diabetic macular edema)

The CHMP of the EMA has recommended ranibizumab (LUCENTIS) for approval in the EU for the treatment of vision loss due to diabetic macular edema (DME), Novartis announced on 22 October 2010. The regulatory submission was supported by results from two phase III trials in patients with DME conducted in Europe, and a phase III trial conducted in the USA in this indication.

Ranibizumab is a humanized anti-VEGF-A antibody fragment being developed as a once-a-month intravitreal injection formulation for the treatment of wet age-related macular degeneration (AMD), DME and retinal vein occlusion (RVO). The product was launched in the USA for the treatment of wet AMD in June 2006, and has subsequently been made available for the same indication in the EU, Canada, and many other regions worldwide. Ranibizumab was approved in the USA for the treatment of macular edema following RVO in June 2010. Phase III evaluation is ongoing in the USA in DME. In June 2003 Novartis acquired an exclusive license from Genentech, a subsidiary of Roche, to develop and market ranibizumab outside North America for indications related to diseases of the eye.

RIGScan CR

Neoprobe files response to a review letter

Neoprobe announced on 21 October 2010 that it has filed a response with the US FDA to a review letter regarding a BLA for RIGScan CR. The response letter was filed as an initial step to reactivate development of RIGScan CR, which was halted in 1997 when the FDA issued a non-approvable letter. Neoprobe is planning to file an IND application for the biologic component of the technology and, once the FDA has assigned an IND, intends to file a protocol for a phase III trial under a Special Protocol Assessment (SPA). A favorable response to a similar protocol was issued by the EMA in October 2008.

RIGScan CR comprises proprietary radiolabelled (low energy gamma ray emitters) tumor-specific monoclonal antibodies and patented surgical methods for real-time detection of tumor deposits that are not detectable by conventional methods. Patients are injected with a radiolabelled monoclonal antibody prior to surgery; tumors can then be detected with Neoprobe's gamma-detection device.

sunitinib

Pfizer recommended for approval, EU (pancreatic cancer)

On 21 October 2010 the CHMP of the EMA adopted a positive opinion, recommending sunitinib (SUTENT) for the treatment of adults with unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumors with disease progression. Pfizer filed for approval of sunitinib in the treatment of pancreatic neuroendocrine tumors in the USA, EU and Canada in January 2010.

Sunitinib is an orally available inhibitor of VEGFR (vascular endothelial growth factor receptor), PDGFR (platelet-

derived growth factor receptor), and KIT and FLT3 tyrosine kinases. The agent was first launched in February 2006 in the USA for the treatment of malignant gastrointestinal stromal tumors (GIST) and metastatic renal cell carcinoma (RCC) in patients intolerant or unresponsive to standard therapies. Sunitinib has subsequently been launched in the EU and many other major markets for the treatment of GIST and RCC. Clinical evaluation of the agent is ongoing for the treatment of other solid tumor types.

FLUENZ

MedImmune recommended for approval, EU (influenza)

The CHMP of the EMA announced on 21 October 2010 that it has adopted a positive opinion, recommending that marketing authorization be granted for MedImmune's trivalent seasonal influenza vaccine (FLUENZ) for prophylaxis of influenza in subjects aged two to 18 years. As part of the marketing authorization, a pharmacovigilance plan will be implemented.

FLUENZ contains cold-adapted, live attenuated influenza viruses that induce a response against influenza A/H3N2, A/H1N1 and B strains. The vaccine is marketed in the USA under the trade name FluMist.

Licensing

AKP 002

Astellas, ASKA licensing agreement

On 19 October 2010 Astellas and ASKA announced that they have entered into a licensing agreement, under which Astellas acquires exclusive worldwide development, manufacturing and commercialization rights for AKP 002. ASKA retains co-promotion rights in Japan, and will receive an upfront fee, development milestone payments and royalties on sales from Astellas. A phase I trial is under way to assess AKP 002 as a treatment for the functional symptoms of benign prostatic hyperplasia.

APC 100 & APC 200

Adamis completes acquisition of licensing agreements

On 19 October 2010 Adamis announced that it has completed the acquisition of exclusive licensing agreements for APC 100 and APC 200, which have potential in the treatment of prostate cancer. A definitive agreement was signed with Colby to acquire the agents in February 2010, under which Colby will be granted 7.5 million shares of Adamis common stock.

APC 100, an anti-androgenic, anti-inflammatory, multi-targeted signal transduction inhibitor, is planned to enter into phase I/II trials in patients with castrate-sensitive or castrate-resistant prostate cancer in 2010. APC 200, a polyamine oxidase inhibitor, is being developed for the treatment of patients with prostate cancer for whom androgen-deprivation therapy may not be approved or appropriate.

drug design technology, DART, MacroGenics

Pfizer, MacroGenics licensing agreement

Boehringer Ingelheim, MacroGenics licensing agreement

On 26 October 2010 MacroGenics announced that it has entered into two agreements concerning its Dual-Affinity Re-Targeting (DART) platform. The technology can be used to develop dual specificity 'antibody-like' scaffold proteins that are capable of targeting multiple receptors with a single molecule. This approach is flexible, allowing divalent and tetravalent targeting possibilities.

A global research collaboration and license agreement has been signed with Pfizer, to discover, develop and commercialize DART products targeting two undisclosed cancer targets. Pfizer will make an upfront cash payment and provide research funding to MacroGenics, which will also be eligible to receive escalating preclinical, clinical, regulatory and commercial milestone payments, in addition to royalties on sales of any products that arise from the collaboration. Further details were not disclosed.

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The second agreement, announced jointly by MacroGenics and Boehringer Ingelheim, covers a global alliance between the two companies to discover, develop and commercialize therapeutics based on MacroGenics' DART platform. Candidates directed against up to ten combinations of molecular targets will be developed, and may span multiple therapeutic areas, including immunology, oncology, and respiratory, cardiometabolic and infectious diseases. Under the terms of the agreement, both companies will share responsibility for discovery and certain preclinical activities, with Boehringer Ingelheim taking sole responsibility for subsequent preclinical, clinical, regulatory, commercial and manufacturing activities. MacroGenics expects to receive payments of approximately US$60 million in the first three years of the collaboration, including an upfront cash payment, annual maintenance fees, R&D funding and near-term research-based milestones. In addition, Boehringer Ingelheim intends to make a future equity investment in MacroGenics. In the eventuality of all ten DART programs achieving full commercial success, MacroGenics stands to receive up to US$210 million for each program from development, regulatory and commercial milestone payments. The company is also eligible for tiered royalties on net product sales, and has the option to co-promote certain DART products in the USA.

DREAM targeted pain therapy, Apeiron

Evotec, Apeiron licensing agreement

Evotec announced on 27 October 2010 that it has entered into a collaborative agreement with Apeiron for the identification of small molecule modulators of the DREAM (Downstream Regulatory Element Antagonistic Modulator) target. Evotec will apply its expertise in cellular assay development to move the project into the hit identification stage and beyond. No financial details of the agreement were disclosed.

DREAM, a calcium regulated transcriptional repressor protein, controls the expression and production of prodynorphin, as well as the expression of opioid receptors in spinal cord neurons. The program to develop pain therapeutics against the DREAM target is utilizing a concept based on research conducted at the Institute for Molecular Biotechnology of the Austrian Academy of Sciences (IMBA). Discovery stage research is ongoing.

drug delivery system, MEDUSA extended-release interferon beta-1a, Merck Serono/Flamel Technologies

Flamel Technologies, Merck Serono milestone payment

Flamel Technologies reported on 19 October 2010 that it has achieved a clinical development milestone under a licensing agreement with Merck Serono (signed in December 2007) to develop an extended-release formulation of interferon beta-1a. This milestone has triggered a EUR3 million payment from Merck Serono to Flamel Technologies. The formulation uses Flamel Technologies' MEDUSA technology, a self-assembled poly-amino acid nanogel system.

drug delivery system, stroke therapy, NeuroVive/to-BBB

NeuroVive and to-BBB establish collaboration

NeuroVive announced on 25 October 2010 that it has entered into a collaborative agreement with to-BBB to develop treatments for stroke and other acute neurodegenerative diseases. Under the terms of the agreement, development activities up to preclinical proof-of-concept will be funded by NeuroVive; the companies will then develop and commercialize the product jointly. The collaborative program will utilize NeuroVive's ciclosporin-based agents and to-BBB's proprietary G-Technology, which can enhance drug penetration across the blood-brain barrier.

fipamezole

Valeant, Santhera licensing termination

Santhera announced on 25 October 2010 that Biovail (a wholly-owned subsidiary of Valeant) has returned US and

Canadian rights to fipamezole following a post-merger pipeline review. Santhera will regain rights to the agent, and all data generated by Biovail, in January 2011.

Fipamezole, a specific alpha$_2$ adrenergic antagonist, is in development for the treatment of levodopa-induced dyskinesia in patients with Parkinson's disease. Phase II trials have been conducted, and Santhera intends to conduct phase III evaluation of the agent in North America.

gene therapies, GlaxoSmithKline/ Telethon/San Raffaele Del Monte Tabor Foundation

GlaxoSmithKline, Telethon, San Raffaele Del Monte Tabor Foundation licensing agreement

On 18 October 2010 GlaxoSmithKline, Telethon (Italy) and the San Raffaele Del Monte Tabor Foundation (Italy) announced that they have entered into a strategic alliance for the development of ex vivo gene therapies for the treatment of rare genetic disorders. Under the terms of the agreement, GlaxoSmithKline gains an exclusive license for the development of a gene therapy for ADA Severe Combined Immune Deficiency (ADA-SCID), as well as rights to co-develop with Telethon and the San Raffaele Del Monte Tabor Foundation ex vivo gene therapies for six other rare diseases, including metachromatic leukodystrophy (MLD), Wiskott-Aldrich Syndrome (WAS), beta-thalassemia, mucopolysaccharoidosis type I (MPS), globoid leukodystrophy (GLD) and chronic granulomatous disorder (CGD). Under the terms of the alliance, GlaxoSmithKline will pay Telethon an upfront payment of EUR10 million. Telethon is eligible to receive further payments upon the completion of development milestones.

The ex vivo gene therapies involve the introduction of corrected genes into patients' stem cells using a lentivirus vector developed at HSR-TIGET, a joint venture between Telethon and the San Raffaele Del Monte Tabor Foundation. A phase I/II trial in patients with ADA-SCID has completed and phase I/II trials in patients with WAS and MLD are under way.

glucopyranosyl lipid adjuvant, Immune Design

MedImmune, Immune Design licensing agreement

Immune Design has signed a license and development deal with MedImmune relating to the use and commercialization of glucopyranosyl lipid adjuvant (GLA) in vaccines for specific infectious diseases. The terms of the agreement stipulate that MedImmune acquires exclusive global rights to research, develop, use and commercialize GLA in vaccines for certain disease indications. IDC will receive an upfront license fee and potential development-, regulatory- and commercial-based milestone payments totalling US$212 million, as well as sales-based royalties on products that reach the market.

GLA is a small molecule vaccine adjuvant that acts as a Toll-like receptor 4 (TLR-4) agonist on human dendritic cells.

IPI 940

Mundipharma, Purdue acquire rights to Infinity's FAAH inhibitor program

Infinity announced on 26 October 2010 that Purdue and Mundipharma have acquired worldwide development and commercialization rights to Infinity's fatty acid amide hydrolase (FAAH) program. This follows top-line results from a phase I trial of an FAAH inhibitor from the program IPI 940, which was well tolerated, produced marked FAAH inhibition and showed favorable pharmacokinetics following oral administration in healthy volunteers. Phase I evaluation of IPI 940, which has potential in the treatment of pain and inflammatory diseases, is ongoing. Purdue intends to conduct a phase II trial of the agent in 2011, following the completion of certain development activities by Infinity.

Infinity entered into an agreement with Purdue and its independent associated company Mundipharma in November 2008, granting the companies worldwide rights to the FAAH program after completion of phase I trials. Under the terms of the agreement, Purdue and Mundipharma will now assume research and development costs and Infinity will

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receive global net sales-based royalties for IPI 940 and any other products from the program that reach the market. Infinity will retain commercialization rights in the USA.

Lumi4 complexes

Algeta, Lumiphore licensing agreement

Lumiphore reported on 21 October 2010 that it has signed an agreement with Algeta relating to the use of Lumi4 complexes to develop Algeta's targeted radiotherapeutics and companion diagnostics. The deal includes an option for Algeta to acquire exclusive rights to incorporate Lumi4 into future targeted anticancer radiopharmaceuticals. Algeta will use the Lumi4 complexes in its radioimmunotherapeutic programs that link thorium-227 to tumor targeting agents, such as monoclonal antibodies.

Lumiphore's Lumi4 complexes, a bifunctional metal-chelation technology, can be utilized in the development of therapeutic drugs, imaging agents and diagnostics. The technology is based on a class of metal lanthanide and actinide chelators; a novel cage structure surrounds lanthanide ions, allowing them to be tightly held and covalently attached to receptor targeting molecules. Lumi4 complexes can be used to chelate radioactive metal isotopes and covalently attach them to therapeutic antibodies, peptides, proteins or other receptor-targeting agents for enhanced targeted delivery to cancer cells.

obinutuzumab & ocrelizumab

Genentech, Biogen Idec licensing agreement modified

On 21 October 2010 Biogen Idec and Genentech announced that they have restructured their collaboration regarding anti-CD20 antibodies. Genentech will be responsible for the development and commercialization of ocrelizumab for the treatment of multiple sclerosis, and will fund 100% of development costs going forward. Tiered, double-digit royalties on US sales of the compound will be paid to Biogen Idec, which will approximate the company's previous 30% interest in the agent. The current profit share of rituximab (RITUXAN) will not be affected by the commercialization of ocrelizumab.

The companies also agreed that Biogen Idec's share of the profits and losses related to the development and commercialization of obinutuzumab (GA 101) in the USA will be increased from 30% to 35%. A US$10 million catch-up payment will be made by Biogen Idec to Genentech to cover expenses incurred during the period of development when Biogen Idec was paying 30% of costs. Upon the achievement of certain sales milestones for obinutuzumab, Biogen Idec's share of the co-promotion profits for rituximab will decrease from 40% to 35%.

Obinutuzumab, a humanized IgG1-type monoclonal antibody that binds to the extracellular part of the human CD20 antigen on malignant human B cells, is being developed by Roche, Genentech and Biogen Idec for the treatment of cancer. Phase III trials evaluating the agent in patients with indolent non-Hodgkin's lymphoma and chronic lymphocytic leukemia (CLL) are under way. Ocrelizumab, a humanized monoclonal antibody targeting CD20, is undergoing phase II evaluation for the treatment of relapsing-remitting multiple sclerosis.

RX 10045

Resolvyx, Celtic Therapeutics sign option agreement

Resolvyx and Celtic Therapeutics have entered into an option agreement for RX 10045 whereby Celtic Therapeutics has gained an exclusive option to acquire and license rights to the agent for all ophthalmic indications, the companies announced on 26 October 2010. Celtic Therapeutics has also gained an option to license a second compound from Resolvyx in a topical formulation for development in ophthalmic indications. As part of the option agreement, Celtic Therapeutics purchased a note convertible into Resolvyx equity.

Resolvyx is developing RX 10045, an isopropyl ester prodrug of the active resolvin RX 10008, for the topical treatment of chronic dry eye syndrome. A phase I/II trial of RX 10045 has been conducted in the USA in patients with moderate-to-severe dry eye syndrome, and a randomized, placebo-controlled phase III trial of the agent is expected to initiate in 2011.

vaccine, malaria, Cytos/NIH

National Institutes of Health, Cytos licensing agreement

Cytos announced on 21 October 2010 that it has been awarded a subcontract from Science Applications International Corporation (SAIC) to support the preclinical development of a malaria vaccine in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) of the US National Institutes of Health (NIH). Cytos is providing its virus-like particle (VLP)-based vaccination technology to the program; the NIH is providing malaria antigen candidates. Vaccines generated by Cytos will be evaluated in preclinical models of malaria by SAIC and the NIH. SAIC is project managing the program and providing research, development, product and regulatory services and support to the NIH. Funding support is being provided by the NIAID.

Technology Transfer Spotlight

Opportunities with Cancer Research Technology

drug design technology, DNA fusion vaccines, Cancer Research Technology

Cancer Research Technology partnering opportunity, Worldwide

Cancer Research Technology has developed a DNA fusion vaccine technology with potential in the treatment of cancer and infectious diseases. The DNA vaccine technology comprises a specific tumor antigen (epitope) fused to an immunoenhancing sequence, which serves to promote the immune response to the DNA vaccine by inducing CD4+ helper T cells, and by activating high levels of antitumor antibody or cytotoxic CD8+ T cells. Immunoenhancing sequences which may be incorporated into the vaccines include Fragment C of tetanus toxin (FrC) or domain 1 of Fragment C (pDOM). Phase I/II clinical trials of vaccines incorporating a number of different tumor antigen-immunoenhancing sequence combinations have been conducted in lymphoma, myeloma, prostate cancer and colorectal cancer; the trials confirmed the safety and immunogenicity of the vaccines. Phase II evaluation is ongoing. Cancer Research Technology is seeking partnering or licensing opportunities to aid further development of its DNA fusion vaccines program.

For further information on the opportunities available, contact:

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MDM2-p53 inhibitors, Cancer Research Technology

Cancer Research Technology partnering opportunity, Worldwide

Cancer Research Technology is seeking collaborative or licensing partners for a program to develop small molecule inhibitors of the MDM2-p53 pathway with potential in the treatment of cancer. The agents inhibit the protein-protein interaction between p53, a tumor suppressor, and MDM2, an oncoprotein which blocks the ability of p53 to activate transcription and targets the molecule for ubiquitin-mediated destruction. A lead isoindolinone from the program showed activity at a concentration less than 50 nM in a p53-MDM2 inhibition assay in vitro; four other compounds from this isoindolinone series showed IC_{50} values between 225 and 435 nM. The program is being conducted under a collaboration between the Cancer Research Technology, De Novo and the Northern Institute for Cancer Research at the University of Newcastle Upon Tyne (UK).

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target, CLEC9A, Cancer Research Technology

Cancer Research Technology licensing offer, Worldwide

Researchers at Cancer Research Technology (UK) have identified a C-type lectin receptor, CLEC9A (DNGR-1), that is selectively expressed in a subset of dendritic cells that are efficient at cross-presentation of antigens, as a target for antibody-mediated delivery of antigens. Proof-of-principle has been demonstrated in vivo. The target also has relevance in the treatment of diseases caused by pathological response to cell death and autoimmune diseases. Antibody-based inhibition of CLEC9A inhibits the response to necrotic cell death, and anti-CLEC9A conjugated antigens can result in antigen tolerance when delivered in the absence of adjuvants.

Cancer Research Technology is seeking to out-license the CLEC9A target under field-specific licenses for use in the development of vaccines for cancer and/or infectious diseases, and for the treatment of autoimmune diseases.

For further information on the opportunities available, contact:

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Products & Biotechnology

neuregulin glial growth factor-2

Acorda preclinical data

Acorda reported preclinical data on 19 October 2010 for neuregulin glial growth factor 2 (GGF2) evaluated in a permanent middle cerebral artery occlusion (MCAO) stroke model. Results showed that iv GGF2 administered once daily for ten days, starting one hour following occlusion, improved recovery of neurological function. When GGF2 dosing was started at one, three or seven days following MCAO, a recovery in neurological function was also observed. Recovery was assessed by a series of sensory and motor tests performed one day prior to, and at one, three, seven, 14 and 21 days after, MCAO.

GGF2 is being developed for the treatment of chronic heart failure and neurological disorders. The agent, which was selected as the lead molecule in Acorda's neuregulin program, acts directly on cardiomyocytes, promoting the repair of tissue damage as a result of heart disease or injury. Acorda intends to conduct a phase I trial of GGF2 in patients with heart failure.

18F-FPPRGD2

Stanford University clinical data

On 20 October 2010 the Canary Foundation at Stanford University (USA) announced that the imaging agent 18F-FPPRGD2 is undergoing a clinical trial in the USA for the detection of lung nodules. In healthy volunteers, there was a low background signal in the thorax using 18F-FPPRGD2, allowing for high tumor-to-background contrast ratio in the lungs. The imaging agent targets the integrin receptor alfavbeta3.

ALKS 33

Alkermes clinical data (Phase I) (drug addiction)

Alkermes has conducted a randomized, double-blind, placebo-controlled, multidose phase I trial that assessed the safety, tolerability and pharmacodynamic effects of ALKS 33 (RDC 0313) and buprenorphine when administered alone and in combination to 12 opioid-experienced users. On 25 October 2010 the company reported top-line results from this trial, which showed that ALKS 33 blocked in a dose-related manner the objective and subjective measures of opioid agonism of buprenorphine. The therapy was generally well tolerated.

ALKS 33, a small molecule, oral opioid receptor modulator, is being developed by Alkermes for the treatment of reward disorders such as addiction. A phase II trial of ALKS 33 in patients with alcohol dependence initiated in November 2009. Alkermes plans to initiate a phase IIa trial in first half 2011 to evaluate ALKS 33 administered in combination with buprenorphine; the trial will be funded by a grant of up to US$2.4 million from the National Institute on Drug Abuse, part of the National Institutes of Health (NIH;USA).

APD 916

Arena clinical data (Phase I)

Arena reported results on 20 October 2010 from a phase I trial to evaluate the safety and pharmacokinetic profile of APD 916 in 24 healthy volunteers. Subjects received a single dose of APD 916 at 1, 3 or 5 mg, or placebo. Results showed that APD 916 exhibited pharmacokinetic exposure proportional to dose, and a terminal half-life of approximately 50 h. All adverse events were mild-to-moderate. Insomnia was commonly reported at a dose of 1 mg. At 3 and 5 mg doses, insomnia, headache, parosmia, alteration in the perception of body temperature, abnormal dreams, and visual and tactile hallucinations were commonly reported. At 5 mg APD 916, CNS-related dose-limiting adverse events included insomnia, abnormal dreams and a nightmare. No significant safety issues were reported with respect to vital signs, ECGs or laboratory testing.

APD 916 is an orally available histamine H3 receptor inverse agonist being developed for the treatment of narcolepsy with cataplexy.

ataluren

PTC Therapeutics phase change II, Europe (metabolic disease)

PTC Therapeutics reported on 26 October 2010 that it has begun a multicenter, open-label, dose-ranging phase II trial in Europe to assess ataluren in 18 patients aged two years or above with nonsense mutation methylmalonic acidemia (nmMMA). The trial aims to determine whether the agent reduces plasma methylmalonic acid levels.

Ataluren is being developed for the treatment of genetic disorders caused by nonsense mutations. The agent allows the translation process to bypass the mutation, restoring the production of full-length functional proteins. Phase III evaluation of ataluren is under way in patients with cystic fibrosis and phase II evaluation is ongoing in Duchenne/Becker muscular dystrophy and hemophilia.

beta-secretase inhibitor, AstraZeneca/Astex Therapeutics

AstraZeneca, Astex Therapeutics preclinical evaluation, UK (Alzheimer's disease)

AstraZeneca, Astex Therapeutics milestone payment

Astex Therapeutics announced on 25 October 2010 that AstraZeneca has selected a development candidate under the companies' collaborative drug discovery program to identify small molecule beta-secretase inhibitors with potential in the treatment of Alzheimer's disease. The candidate selection has triggered an undisclosed milestone payment from AstraZeneca to Astex Therapeutics. The latter is eligible to receive clinical development-based milestone payments and royalties following commercialization of any products arising from the collaboration. No financial details were disclosed.

AstraZeneca and Astex Technology (now Astex Therapeutics) entered into the collaboration agreement in March 2003.

See R&D Focus (Drug Updates) for full product details

Under the collaboration, Astex Therapeutics has utilized its Pyramid fragment-based drug discovery technology platform to identify inhibitors of beta-secretase, an enzyme implicated in the progression of Alzheimer's disease. AstraZeneca is responsible for clinical development and commercialization of the selected candidate drug.

CAL 101

Calistoga phase change II, USA (CLL, lymphoma)

Calistoga announced on 19 October 2010 that a phase II trial has initiated in the USA to evaluate the safety and efficacy of CAL 101, in combination with rituximab, in previously untreated elderly patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). The trial will enroll up to 60 patients over 65 years of age who will receive CAL 101, administered orally twice a day in combination with rituximab administered in eight weekly doses, and will remain on the treatment as long as they continue to benefit. Patients will not receive chemotherapy.

CAL 101 is an oral small molecule inhibitor of the delta isoform of PI3-kinase (p110delta) being developed for the treatment of hematological cancers. Phase I evaluation of the agent as monotherapy is ongoing in the USA in patients with CLL, indolent non-Hodgkin's lymphoma (iNHL), or mantle cell lymphoma. A phase I trial of CAL 101 in combination with rituximab and bendamustine in patients with iNHL or CLL is also ongoing in the USA.

CERE 120

Ceregene initiates enrollment in phase II part of trial

Ceregene announced on 19 October 2010 that it has begun enrolling patients in the phase IIb part of an ongoing double-blind, sham surgery-controlled, US phase I/IIb trial of CERE 120. Early safety was demonstrated in the phase I portion of this study, which is evaluating an enhanced dosing regimen of the agent that targets the terminals of degenerating dopamine neurons in the putamen, and the cell bodies of these neurons in the substantia nigra.

CERE 120 comprises an adeno-associated serotype 2 viral (AAV2) vector encoding human neurturin. The natural prepro domain of neurturin has been replaced with human beta nerve growth factor (NGF) to promote secretion of mature neurturin from transduced cells.

ChronVac-C

ChronTech clinical data (Phase I/II) (hepatitis C)

ChronTech reported results on 25 October 2010 from a phase I/IIa trial of ChronVac-C followed by standard of care (PEGylated interferon and ribavirin), conducted in Sweden in patients with hepatitis C virus (HCV) infection. Results showed that of seven patients who received ChronVac-C followed by standard of care, five patients (71%) had less than 50 virus copies/mL blood at week four, five patients were negative for HCV RNA at week 12, and six patients (85%) were negative for HCV at week 24. ChronTech intends to submit an application to the Swedish Medical Product Agency to conduct a phase IIb trial of ChronVac-C in patients with HCV infection; ChronVac-C treatment will be followed by standard of care and compared with standard of care treatment alone.

ChronVac-C is a therapeutic gene-based (DNA plasmid) vaccine for the treatment of chronic HCV infection. The vaccine utilizes Inovio Pharmaceuticals' proprietary MEDPULSER DNA delivery system for in vivo electroporation delivery of the vaccine.

clazosentan

Actelion discontinues enrollment into phase III trial

Actelion reported on 21 October 2010 that, following discussions with the trial's steering committee, it has discontinued patient enrollment into the CONSCIOUS-3 phase III trial of clazosentan in patients with non-traumatic subarachnoid hemorrhage. The steering committee reviewed this trial after the failure of the primary endpoint (announced in September 2010) in the CONSCIOUS-2 phase III trial of clazosentan. Both phase III trials were designed to assess the preventative effects of clazosentan

in vasospasm-related morbidity and all-cause mortality after aneurysmal subarachnoid hemorrhage. Actelion is collecting and analyzing results from the CONSCIOUS-3 trial and other trials of clazosentan, an injectable endothelin A antagonist.

CYT 107

Cytheris initiates phase II trial in HIV-infected patients

Cytheris announced on 19 October 2010 the initiation of a randomized, noncomparative controlled, multicenter phase II trial, designated ERAMUNE 01, to evaluate CYT 107, in combination with the integrase inhibitor raltegravir and the CCR5 inhibitor maraviroc, in HIV-infected patients with long-term viral suppression. The aim of the trial, which will enroll 28 patients (selected on the basis of a low peripheral blood reservoir) at centers in France, Italy, Spain and the UK, is to determine the feasibility of exhausting the HIV reservoir and achieving virus eradication. Patients will be randomized in an open-label, nonblind manner to one of two cohorts. The first will receive highly active antiretroviral therapy (HAART) comprising current ART in combination with raltegravir and maraviroc; the second will receive HAART for eight weeks, and will then receive two cycles of CYT 107 injections in addition to HAART. The primary objective of the trial will be to show an important decrease in the HIV-1 viral reservoir; secondary objectives include eradication of HIV in the lymphoid reservoirs of HIV in the gut, and evaluation of the safety and immunologic effects of treatment intensification with or without immunomodulatory therapy.

CYT 107 is a recombinant human interleukin-7 (rIL-7) being developed for the treatment of cancer, hepatitis C virus (HCV) infection, hepatitis B virus (HBV) infection, and for use in immunocompromised patients, including patients undergoing cancer treatment, recovering from bone marrow transplant, and HIV-infected patients. Two other phase II trials of the agent, designated INSPIRE 2 and INSPIRE 3, in chronically HIV-1-infected patients are ongoing in North America, and Italy, Switzerland and South Africa, respectively.

CytoFab

AstraZeneca initiates phase II trials (sepsis, septic shock)

On 25 October 2010 BTG announced that AstraZeneca has initiated dosing in a worldwide phase IIb trial of CytoFab (AZD 9773), an ovine polyclonal antibody targeted against tumor necrosis factor alpha (TNF-alpha), in adults with severe sepsis and/or septic shock receiving best supportive care. The randomized, double-blind, placebo-controlled trial will evaluate the efficacy and safety of two iv dosing regimens of CytoFab in 300 patients. The primary outcome measure will be number of ventilator-free days over a 28-day period following the first dose of CytoFab. Secondary outcome measures include patient mortality at seven and 28 days, and safety and tolerability of the agent.

BTG also reported that AstraZeneca has initiated a dose-escalation phase II trial of CytoFab in Japan to evaluate the safety, tolerability and pharmacokinetics of iv infusions of CytoFab in Japanese patients with severe sepsis and/or septic shock. AstraZeneca acquired worldwide development and marketing rights to CytoFab for all indications from Protherics (now BTG) in December 2005.

DCCR

Essentialis receives SPA agreement from FDA for phase III trial

Essentialis reported on 25 October 2010 that it has reached an agreement with the US FDA on a Special Protocol Assessment (SPA) for a double-blind, placebo-controlled, active-controlled phase III trial to assess two doses of DCCR (diazoxine choline controlled release) in the treatment of patients with hypertriglyceridemia. Half of the patients in the trial will be co-administered statin therapy. The percentage change from baseline in triglyceride levels is the primary endpoint of the trial. Percentage changes in non-HDL cholesterol and ApoB levels are among the secondary endpoints. Exploratory endpoints include non-lipid cardiovascular risk factors, including blood pressure and waist circumference. Efficacy endpoints will be assessed at 12 weeks. The trial includes a 40-week safety extension stage in which placebo-treated patients will switch to active control.

See R&D Focus (Drug Updates) for full product details

DCCR, a once-daily tablet formulation of diazoxide choline (an ATP-dependent potassium channel agonist), has been evaluated in a phase II trial in patients with hypertriglyceridemia and mixed dyslipidemia.

deforolimus

ARIAD clinical data (Phase II) (endometrial cancer)

ARIAD reported interim results on 25 October 2010 from a phase II trial of oral deforolimus in patients with metastatic or recurrent endometrial cancer. In this safety and efficacy trial, patients received oral deforolimus, oral progestin, or chemotherapy. Results from the trial, based on 114 patients enrolled in the USA and Europe, showed that the primary endpoint was met; there was a statistically significant improvement in progression-free survival in patients receiving deforolimus (3.6 months), compared with those receiving standard of care (1.9 months; p=0.007). There was a significantly higher incidence of serious adverse events in patients receiving deforolimus (23.6%) compared with those receiving standard of care (3.8%). The most common adverse events associated with deforolimus treatment were mucositis (38.2%), stomatitis (21.8%) and hyperglycemia (27.3%). Based on these results, Merck & Co has ceased further enrollment in the trial and is monitoring surviving patients.

Merck & Co and ARIAD are developing deforolimus (ridaforolimus), a rapamycin analogue and inhibitor of mTOR (mammalian target of rapamycin) as an oral and iv therapy for cancer. A global phase III trial of oral deforolimus is ongoing in patients with metastatic soft tissue and bone sarcomas. Phase II trials of oral deforolimus are ongoing in advanced nonsmall cell lung cancer (NSCLC) and HER2-positive breast cancer. Phase II trials of an iv formulation are under way in the USA in patients with relapsed or refractory hematological cancer, solid tumors, prostate cancer and endometrial cancer. ARIAD entered into a global agreement with Merck & Co to jointly commercialize and develop deforolimus in July 2007; this agreement was restructured in May 2010.

dimiracetam

Neurotune clinical data (Phase II) (neuropathic pain)

Neurotune reported top-line results on 21 October 2010 from a phase II safety and efficacy trial of dimiracetam (NT 11624) conducted in South Africa in patients receiving antiretroviral therapy for AIDS who had painful neuropathy. In this eight-week trial, 116 patients received a twice-daily oral dose of 400 mg dimiracetam, or placebo, which was doubled every two weeks to a maximum dose of 1600 mg bid (if the previous dose did not cause tolerability problems). Preliminary evidence for efficacy was sought by evaluating pain intensity at the start and end of the study, assessed by the Visual Analogue Scale (VAS) and the Total Symptoms Score (TSS). Results showed that dimiracetam was safe and well tolerated; no safety concerns were observed in 111 patients who reached and maintained the highest dose of the agent to the end of the study. There was no difference between the study groups in terms of the patients' general health (as assessed by the Clinical Global Impression (CGI) scale), or severity of their AIDS (as assessed by viral load and CD4+ count). Five patients discontinued the trial for reasons unrelated to dimiracetam treatment. A high placebo effect and a compliance failure prevented an initial assessment of efficacy; however, post-hoc analysis showed that patients receiving 1600 mg dimiracetam, who had adequate blood levels of the agent, showed significantly greater pain relief (as assessed by TSS), compared to those with suboptimal blood levels.

Dimiracetam is a small molecule, subtype-selective NMDA receptor antagonist being developed as an oral therapeutic for HIV-associated pain and osteoarthritic pain. Neurotune intends to conduct a pivotal phase II trial of dimiracetam in patients with HIV. The company acquired rights to dimiracetam from Brane Discovery in September 2008.

drug delivery system, liposomal ciprofloxacin, Aradigm

Aradigm clinical data (Phase II) (bronchiectasis)

Aradigm reported on 20 October 2010 data from the completed six-month ORBIT-2 phase IIb trial of its dual-

release ciprofloxacin for inhalation (DRCFI;ARD 3150) in patients with non-cystic fibrosis bronchiectasis. In the trial, 42 patients were randomized 50:50 to receive this liposomal-encapsulated ciprofloxacin or placebo, once daily for 28 days, before a 28-day off-treatment period; this cycle was repeated three times. The trial's primary endpoint, mean change in Pseudomonas aeruginosa density in sputum from baseline to day 28, was met; there was a mean reduction of 4.2 $\log_{10}$ units (nearly a sixteen-thousand fold decrease in bacterial load) in the liposomal ciprofloxacin group and a decrease of 0.1 $\log_{10}$ units in the placebo group (p=0.004) in the full analysis population (randomized patients who received at least one dose and provided samples for at least two time-points). Among secondary endpoint analyses, supplemental antibiotics for respiratory-related infections were needed by 17 patients in the placebo group and eight patients in the liposomal ciprofloxacin group (p=0.05). Median time to first exacerbation was 134 days and 58 days in the treatment and placebo groups, respectively, with fewer exacerbations in the liposomal ciprofloxacin group compared with the placebo group. The agent showed good tolerability. No significant decreases in lung function (measured by FEV_1) at 28 days were observed in either group. The overall rate and severity of adverse events was similar in both groups.

Inhaled liposomal-encapsulated ciprofloxacin is being developed for the treatment of bacterial infections in cystic fibrosis patients under the program code ARD 3100, and for infections associated with non-cystic fibrosis bronchiectasis under the code ARD 3150. The agent is also being evaluated for the treatment of inhalation anthrax under the code ARD 1100.

drug delivery system, transdermal interferon alfa-2b, Helix BioPharma

Helix BioPharma IND submission, USA (genital warts)

Helix BioPharma announced on 19 October 2010 that it has submitted an IND to the US FDA seeking approval to conduct a phase II/III trial of interferon alfa-2b in patients with cervical intraepithelial neoplasia grade 1 or 2 lesions (CIN 1 or CIN 2, respectively). This randomized, double-blind, vehicle-controlled, efficacy trial plans to enroll 492 premenopausal subjects who will self-administer the agent, or control, topically every other day (except during menstruation) until 35 doses have been applied over a period of ten to 14 weeks; the overall treatment and follow-up period will be 12 months. The proposed primary endpoint will be resolution of CIN 1 or CIN 2 after 12 months, as determined by cervical biopsy and Pap smear. Helix BioPharma is also planning to conduct a phase III efficacy trial of the agent in Europe in this indication.

Helix BioPharma is developing a transdermal system for the administration of interferon alfa-2b, using the company's proprietary BIPHASIX microencapsulation technology, for the treatment of cervical dysplasia and anogenital warts. A phase II trial, to evaluate the safety, efficacy and pharmacokinetic profile of the agent in women with low-grade squamous intraepithelial lesions has been conducted in Germany.

eculizumab

Alexion clinical data (Phase II) (atypical hemolytic uremic syndrome)

Alexion reported results on 20 October 2010 from phase II trials of eculizumab (SOLIRIS) being conducted in the USA, Canada and the EU in adult and adolescent patients with atypical hemolytic uremic syndrome (aHUS). In a trial in patients resistant to plasma therapy, interim results for 17 patients treated for up to 26 weeks showed that the primary endpoint was met; there was a significant increase in platelet count (a measure of thrombotic microangiopathy; TMA) of 80 000 +/- 64 000/mcL, compared to baseline (p less than 0.0001). In a trial in 20 patients who were receiving chronic plasma therapy prior to the study, interim results for 15 patients treated for at least 12 weeks also showed that the primary endpoint was met; a significant proportion of patients (87%) achieved TMA event-free status, as defined by stable platelet counts, absence of plasma therapy and no new dialysis. Key clinical secondary endpoints were also met in both trials. Eculizumab was well tolerated in both trials. Adverse events most commonly observed included anemia, diarrhea, headache, nausea and hypertension.

See R&D Focus (Drug Updates) for full product details

Eculizumab is a humanized monoclonal antibody targeted to complement C5 being developed for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) and aHUS. The antibody is designed to inhibit complement activation with a prolonged duration of action. Eculizumab is marketed in the USA and a number of EU countries for the treatment of PNH. Phase II evaluation is ongoing in North America and the EU in the treatment of aHUS, including a trial in pediatric patients. Phase II trials have also been conducted in the USA in the treatment of rheumatoid arthritis and nephritis.

enclomifene

Repros Therapeutics phase change II, USA (diabetes)

On 25 October 2010 Repros Therapeutics announced that it has started randomizing patients into a phase II trial of enclomifene (ANDROXAL). Up to 150 patients with secondary hypogonadism or adult-onset idiopathic hypogonadotrophic hypogonadism, who also have type II diabetes, will be enrolled. The study will assess the ability of the agent to improve glycemic control in this population. Interim data from the first 60 patients to complete the trial are expected to be reported during second quarter 2011, with complete results anticipated before end 2011.

Enclomifene, a once-daily, centrally acting oral therapy that increases certain hormones that stimulate the production of testosterone, is being developed for the treatment of hypogonadism. A phase III trial of the agent for the treatment of testosterone deficiency resulting from secondary hypogonadism has been conducted in the USA.

GSK 1349572

Shionogi, ViiV Healthcare phase change III (HIV infection)

Shionogi-ViiV Healthcare, a joint venture between Shionogi and ViiV Healthcare, announced on 21 October 2010 that it has initiated a phase III program to investigate the safety and antiviral activity of GSK 1349572, in comparison with raltegravir, in HIV-infected patients. Two randomized, blinded, active-controlled, parallel group, multicenter, non-inferiority trials are being conducted. The first trial, designated SPRING-2, will enroll an estimated 788 treatment-naive HIV-1-infected patients, and will compare the safety and efficacy of once-daily GSK 1349572 dosed at 50 mg with raltegravir 400 mg bid, both administered for 48 weeks with investigator-selected dual nucleoside reverse transcriptase inhibitor therapy. The primary endpoint will be antiviral activity; secondary endpoints will be antiviral activity at 96 weeks, tolerability, long-term safety, immunologic activity, and viral resistance in subjects experiencing virologic failure.

The second trial, designated SAILING, will enroll an estimated 688 integrase-naive HIV-1-infected patients who have previously received HIV therapy, and will compare the safety, efficacy and pharmacokinetic profile of once-daily GSK 1349572 dosed at 50 mg with raltegravir 400 mg bid, both administered in combination with a background regimen comprising one or two fully active agents at 48 weeks. The primary endpoint will be antiviral activity; secondary endpoints will be long-term antiviral activity, pharmacokinetics, the relationship between pharmacokinetics and antiviral activity, and safety and tolerability.

GSK 1349572 (S 349572) is an oral HIV integrase inhibitor that is being developed for the once-daily treatment of HIV infection. Two phase IIb trials of the agent, in treatment-naive and treatment-experienced (raltegravir-resistant) patients, respectively, have completed in the USA and Europe. ViiV Healthcare was formed in October 2009 when GlaxoSmithKline and Pfizer completed an agreement to combine their HIV/AIDS therapy businesses.

IC41 & nitazoxanide

Romark, Intercell trial planned (Phase II), Europe (hepatitis C)

On 21 October 2010 Intercell and Romark announced that they are planning to conduct a phase II trial of a combination therapy of Intercell's hepatitis C virus (HCV) vaccine candidate, IC41, and Romark's nitazoxanide, a thiazolide, in treatment-naive patients with chronic HCV genotype 1 infection. The trial is expected to enroll 60 patients in Europe who will receive IC41 plus nitazoxanide, IC41 plus nitazoxanide and peginterferon alfa-2a, or

standard of care (peginterferon alfa-2a and ribavirin). Sustained virologic response will be the primary endpoint of the trial, which is expected to initiate first half 2011.

IC41 was developed using Intercell's proprietary TRANSVAX technology, and comprises five synthetic peptides (IPEP83, 84, 87, 89, 1426) harboring HCV CD4 and CD8 T-cell epitopes and the synthetic adjuvant poly-L-arginine (IC30). A phase II proof-of-concept trial of IC41 has been conducted. Nitazoxanide has been marketed in several regions for the treatment of parasitic infections and cryptosporidiosis in AIDS patients, and for the treatment of diarrhea caused by Cryptosporidium parvum and Giardia lamblia. Romark is planning to conduct phase III evaluation of nitazoxanide in combination with peginterferon for the treatment of chronic HCV infection. A phase II/III trial has been conducted in chronic HCV-infected patients.

IC43

Intercell clinical data (Phase II) (bacterial infection)

On 25 October 2010 Intercell reported data from a randomized phase II trial that enrolled approximately 400 mechanically ventilated intensive care patients to receive IC43, a Pseudomonas aeruginosa vaccine, on days zero and seven in four treatment groups of 100 or 200 mcg alum-adjuvanted vaccine, 100 mcg non-adjuvanted vaccine, and alum alone as placebo. This trial met its primary endpoint; good seroconversion rates (65-81%) were achieved in all vaccine groups, with IgG antibody geometric mean titers of 995-2117 ELISA units/mL. Secondary immunogenicity endpoints were also met. Patients receiving alum did not demonstrate clear immune-enhancement, whereas immunogenicity following the second vaccination was observed in all vaccine groups, as well as a dose-response. A statistically significant reduction in mortality rate was achieved in the non-adjuvanted vaccine group (21.7% at day 28) compared with the placebo group (40% at day 28; p=0.0196); however, this trial was not powered for efficacy. Treatment-emergent adverse events were not significantly different between the treatment arms, and the number and nature of reported adverse events did not raise safety concerns. The agent appeared to be well tolerated, but tolerability could not be definitively assessed in this population. However, the study did demonstrate the feasibility of assessing the efficacy of the vaccine in this population.

Intercell is developing IC43, a prophylactic vaccine for P aeruginosa infection. The vaccine is a recombinant subunit vaccine that comprises two outer membrane proteins of P aeruginosa, and acts by inducing functional antibodies.

IMO 3100

Idera clinical data (Phase I)

On 21 October 2010 Idera reported results from a single-dose phase I trial of IMO 3100 in healthy volunteers. The agent was well tolerated at all dose levels (0.04-0.64 mg/kg) and no serious adverse events were reported. All adverse events were grade 1, with mild injection site reaction being the most frequent adverse event. TLR7- and TLR9-mediated cytokine induction was inhibited in PBMCs isolated from subjects treated with 0.32 and 0.64 mg/kg IMO 3100. No evidence of cytokine inhibition was observed in placebo-treated subjects. Inhibition of cytokine induction was dose-dependent. The agent inhibited induction of cytokines including TNF-alpha, IL-1beta, IL-6, IL-2R, IL-12, IL-10, IL-8, MIP-1alfa and beta, IFN-alfa and RANTES. Suppression of selected cytokines was observed for up to five days.

Idera also reported that dosing has completed in a multiple-dose phase I trial. Subjects received IMO 3100 via two dosing regimens for four weeks. The trial remains blinded, but no treatment-related discontinuations or serious adverse events were observed in the 24 subjects. Analysis of data from the trial is expected to complete by end 2010.

IMO 3100, a Toll-like receptor 7 and 9 (TLR7 and TLR9) antagonist, is being developed for the treatment of autoimmune diseases.

IW 001

Lung Rx, ImmuneWorks phase change I, USA (pulmonary fibrosis)

ImmuneWorks announced on 19 October 2010 that it has initiated a phase I trial of IW 001 in patients with

idiopathic pulmonary fibrosis (IPF). The trial will be conducted at sites in the USA, and will assess the agent's safety and ability to influence the ongoing immune response in IPF patients.

IW 001, an oral purified bovine type V collagen solution, was granted Orphan Drug designation in the USA for the treatment of IPF in November 2009. ImmuneWorks is developing IW 001 with Lung Rx, a subsidiary of United Therapeutics, under an agreement signed in February 2010.

LY 3009104

Lilly starts phase IIb trial

Incyte, Lilly milestone payment

Incyte announced on 20 October 2010 that its collaboration partner Lilly has initiated a phase IIb trial of LY 3009104 (formerly INCB 28050) in the USA in patients with active rheumatoid arthritis on background methotrexate therapy. Achievement of this milestone has triggered a US$19 million payment from Lilly to Incyte. The randomized, placebo-controlled, double-blind, parallel assignment, dose-ranging study is expected to enroll approximately 270 patients who will receive either 2, 4 or 8 mg of the agent once daily for 24 weeks, or 1 mg of the agent once daily for 12 weeks followed by randomization to either 4 mg once daily or 2 mg twice daily for an additional 12 weeks. The primary outcome measure of the study will be the proportion of patients in the 4 mg and 8 mg dose groups who achieve an American College of Rheumatology (ACR) 20 responder index (ACR20) response. The secondary outcome measures will include the percentage of patients who achieve ACR20, ACR50, ACR70 and ACR50 responder index response.

LY 3009104 is a follow-on compound from Incyte's program of JAK inhibitors. Lilly and Incyte signed an exclusive global license and collaboration deal to develop and commercialize the agent and various follow-on JAK1/JAK2 inhibitors, for the treatment of inflammatory and autoimmune diseases in December 2009. Under the agreement, Incyte has an option to co-develop the JAK1/JAK2 inhibitors on a compound-by-compound and indication-by-indication basis at the start of phase IIb trials.

NGR-hTNF

MolMed phase change II, Italy (soft tissue sarcoma)

MolMed announced on 27 October 2010 that the first patient has been enrolled in a phase II trial of NGR-hTNF (ARENEGYR), designated NGR016, for the treatment of soft tissue sarcoma. The randomized study will assess NGR-hTNF monotherapy, or treatment in combination with doxorubicin, in approximately 96 patients. Outcome measures of the trial will include progression-free survival and tumor metabolic response, as measured by PET scan.

NGR-hTNF, a small recombinant fusion protein, reduces tumor mass by targeting tumor vasculature. NGR-hTNF is a modified form of TNF-alpha fused with NGR peptide. The peptide binds to the CD13 receptor, and has a ten-fold lower toxicity profile than TNF-alpha. A phase III trial of NGR-hTNF in patients with malignant pleural mesothelioma is ongoing in Italy and the USA. Phase II evaluation of the agent is ongoing for the treatment of ovarian cancer, small cell and nonsmall cell lung cancer (NSCLC), and phase II trials have completed in patients with hepatocellular carcinoma, mesothelioma and colorectal cancer.

orBec

Soligenix clinical data (Phase II) (graft versus host disease)

Soligenix reported on 25 October 2010 preliminary results from a phase II trial of orBec in the prevention of acute graft-versus-host disease (GvHD) in 140 patients undergoing myeloablative conditioning regimens. Dosing was started before allogeneic hematopoietic cell transplantation (HCT) and continued through day 75 of the post-transplantation period. Data indicated that orBec showed good safety and tolerability. The trial did not meet its primary efficacy endpoint of a reduction in the proportion of patients who developed acute GvHD with severity sufficient to require systemic immunosuppressive treatment on or before day 90 after transplantation. More severe acute GvHD grades IIb-IV developed in 21% and 33% of patients who received orBec and placebo, respectively (not statistically significant).

orBec a locally acting, oral formulation of beclometasone dipropionate (BDP), consists of two tablets that release BDP in the proximal and distal parts, respectively, of the gastrointestinal tract. The agent is being evaluated in a confirmatory phase III trial in the treatment of acute gastrointestinal GvHD; this trial is expected to complete second half 2011.

QPI 1007

Quark Pharmaceuticals provides update on development

Quark Pharmaceuticals is conducting a dose-escalation phase I trial of QPI 1007, a small interfering RNA (siRNA) molecule, in up to 66 patients with chronic nerve atrophy (legally blind) or recent onset acute non-arteritic anterior ischemic optic neuropathy (NAION). The company reported on 20 October 2010 that the first patient in the NAION arm (which will enroll up to 30 subjects) has been dosed, and that dosing has initiated at the highest planned dose level in the chronic nerve atrophy arm. Enrollment into five of the six chronic nerve atrophy cohorts has completed, with no dose-limiting toxicities observed.

resminostat

4SC clinical data (Phase II) (Hodgkin's lymphoma)

4SC reported on 26 October 2010 initial data from the Simon two-stage design phase II SAPHIRE trial of resminostat (4SC 201) in 33 patients with relapsed or refractory Hodgkin's lymphoma, conducted in Europe. In each two-week treatment cycle, oral resminostat is given once daily for five consecutive days followed by a nine-day treatment-free period; patients will receive six treatment cycles in the main stage of the trial. The primary endpoint of the trial is overall objective response rate (ORR), assessed using computed tomography (CT) combined with positron emission tomography (PET). Antitumor activity was assessed every six weeks. The average treatment duration in the first patient group was nine weeks. Resminostat 600 mg showed good tolerability, with the main side effects being mild-to-moderate gastrointestinal- and hematological-related. Several incidences of anemia were observed, which were considered related mainly to the underlying disease. Resminostat showed good bioavailability and plasma exposure levels were sufficient for good pharmacodynamic activity (inhibition of HDAC). Of 18 patients in the first patient group, two patients achieved a partial response (over 50% reduction in tumor size) and eight patients had stable disease. PET analysis indicated that tumors in nearly all of these patients demonstrated a reduction in metabolic activity; most had a partial metabolic response (over 25% decrease in PET activity). In this trial, the minimum number of five responders required to progress from the first to the second Simon stage was achieved. Enrollment has begun in the 15-patient second Simon stage, which includes an option to increase the daily dose of resminostat from 600 mg to 800 mg.

Resminostat, an oral histone deacetylase (HDAC) inhibitor, is also being evaluated in a phase II trial in patients with hepatocellular carcinoma. 4SC plans to conduct a phase I/II trial of the agent in combination with the FOLFIRI regimen the second-line treatment of colorectal cancer patients with KRAS mutations.

TD 1211

Theravance clinical data (constipation)

Theravance announced results from a phase I and a phase II trial of TD 1211 on 21 October 2010. In a placebo-controlled, double-blind, multiple ascending dose phase I trial in which healthy volunteers received once-daily doses of TD 1211 ranging from 2 to 30 mg, all doses were well tolerated. In a group designed to assess entry of TD 1211 into the CNS, repeat doses of 20 mg did not interfere with morphine's effect on pupil diameter.

In a phase II trial of TD 1211 in 70 noncancer patients with opioid-induced constipation (OIC), the study met its primary endpoint of change from baseline in the average number of spontaneous bowel movements (SBM) per week. Once-daily doses of 5 and 10 mg TD 1211 (the highest doses tested) significantly increased average SBMs per week over a two-week period (3.2 and 4.9 SBMs per week, respectively). Median time to first SBM was 8.6 h for 5 mg TD 1211 and 3.6 h for 10 mg TD 1211, compared with 28.7 h for placebo. TD

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1211 was generally well tolerated; abdominal pain, nausea, vomiting and headache were the most common adverse events and occurred at a higher rate in patients dosed with TD 1211 than those who received placebo. Gastrointestinal adverse events were generally mild-to-moderate and the majority resolved within a few days. Five patients discontinued treatment; no serious adverse events were reported.

Theravance is developing TD 1211, an oral peripherally selective mu-opioid receptor antagonist, for the treatment of OIC. The agent is designed to alleviate the gastrointestinal side effects of opioid therapy, without affecting analgesia.

telaprevir

Vertex, Tibotec conducting phase IIIb trial in HCV infection

Vertex announced on 25 October 2010 the initiation of a randomized, open-label, international phase IIIb trial, designated OPTIMIZE, to evaluate twice-daily dosing of telaprevir in approximately 700 treatment-naive patients with chronic genotype 1 hepatitis C virus (HCV) infection. The aim of the trial is to show noninferiority of twice-daily dosing of the agent compared with dosing three times a day. Patients will receive telaprevir 1125 mg twice daily, or 750 mg three times daily, for the first 12 weeks, in combination with PEGylated interferon alfa-2a and twice-daily ribavirin. The patients' treatment response at week four will be used to determine whether patients should receive PEGylated interferon alfa-2a and ribavirin alone for a further 12 weeks or 36 weeks. The primary endpoint will be sustained viral response (SVR) at 24 weeks following the end of treatment. Patient enrollment in the trial, which will be conducted by Vertex's collaborator Tibotec, is expected to start in November 2010; results are expected in 2012.

Telaprevir is an inhibitor of hepatitis C virus (HCV) NS3-4A proteinase being developed for the treatment of HCV infection. Vertex began a rolling NDA submission to the US FDA for telaprevir as a therapy for HCV infection, in second quarter 2010.

teplizumab

Lilly, MacroGenics suspended (diabetes)

On 20 October 2010 MacroGenics and Lilly announced that an independent data monitoring committee (DMC) has completed its review of one-year safety and efficacy data from the Protege phase II/III trial of teplizumab (MGA 031) in patients with type I diabetes and concluded that the trial did not meet its primary efficacy endpoint; a composite of patients' total daily insulin usage and HbA1c level at 12 months. No unanticipated safety issues were identified. Lilly and MacroGenics have decided to suspend further enrollment and dosing in two other trials; the Protege Encore trial, a phase III trial with the same design as the Protege trial, and the SUBCUE trial, a phase Ib trial of subcutaneous teplizumab.

Lilly and MacroGenics will consider all options for teplizumab, a humanized, Fc-engineered monoclonal antibody targeted to CD3, for the treatment of type I diabetes as well as the impact of the DMC's recommendations on development of the agent for other indications.

teriflunomide

sanofi-aventis initiates international phase III trial (multiple sclerosis)

On 26 October 2010 sanofi-aventis announced that it has initiated a 48-week, randomized, placebo-controlled, international phase III trial, designated TERACLES, to evaluate once-daily teriflunomide 7 and 14 mg as adjunctive therapy to interferon-beta in patients with relapsing multiple sclerosis. An estimated 1455 RMS patients who have been receiving a stable dose of interferon-beta for six months will be enrolled in 28 countries. The primary endpoint is annualized relapse rate, and secondary endpoints include disease activity as measured by MRI, time to disability progression and overall safety. Recruitment is expected to commence before end 2010.

Teriflunomide, an immunomodulator and pyrimidine synthesis inhibitor, is under evaluation in a phase III program as a monotherapy, or in combination with other multiple sclerosis drugs, in patients with relapsing forms of multiple sclerosis.

FLUZONE Quadrivalent

Sanofi Pasteur clinical data (Phase II) (influenza)

Sanofi Pasteur, the vaccines division of sanofi-aventis, reported on 25 October 2010 data from a phase II trial of its quadrivalent inactivated influenza vaccine (FLUZONE Quadrivalent) which contains two strains of influenza type A (H1N1 and H3N2) and two strains of influenza type B (one strain from Yamagata lineage and one strain from Victoria lineage). The study assessed the vaccine in comparison to the trivalent inactivated FLUZONE vaccines licensed for use during the 2008-2009 and the 2009-2010 seasons (the trivalent inactivated vaccines of the 2008-2009 and 2009-2010 seasons contained identical A strains but different B strains). In this trial, rates of solicited injection-site and systemic reactions, unsolicited adverse events and serious adverse events indicated that the quadrivalent and trivalent inactivated vaccines had similar safety profiles. The most frequently solicited injection-site reaction was pain in all groups. Myalgia, headache and malaise were the most frequently reported solicited systemic reactions. Geometric mean HAI antibody titres (GMT), rates of a four-fold rise in HAI titres and the percentage of participants with titers greater than or equal to 1:40 showed that HAI antibody responses were comparable in the three groups. The quadrivalent inactivated vaccine induced statistically non-inferior GMT responses to each A strain and each B lineage strain compared with the control trivalent inactivated vaccine containing the respective strains. Sanofi Pasteur is planning to start a phase III trial of its quadrivalent inactivated vaccine before end 2010.

vaccine, norovirus, LigoCyte

LigoCyte clinical data (Phase I/II)

LigoCyte reported results on 25 October 2010 from a multicenter phase I/II trial of an intranasal norovirus vaccine conducted in the USA in healthy adults. Subjects received two intranasal doses of either vaccine or placebo on days 0 and 21, after which safety and immune responses were evaluated. On or after study day 42, the same subjects were challenged with live norovirus and then followed for post-challenge safety and efficacy. Results for 84 subjects who completed the challenge showed that the vaccine was generally well tolerated and exhibited significant efficacy against any norovirus illness (including mild illness) of 47% (p=0.006) and against norovirus infection of 26% (p=0.046), compared with placebo treatment. The vaccine decreased the incidence of acute gastroenteritis (AGE) from 69.2% to 36.8%, and the incidence of norovirus infection from 82.1% to 60.5%, in the 77 subjects who completed the trial as per the original protocol. There was a significant reduction in the severity of illness in subjects receiving the vaccine (p=0.011), compared with those receiving placebo.

LigoCyte's dry powder intranasal norovirus vaccine formulation is based on virus like particle (VLP) antigens, and utilizes GlaxoSmithKline's Monophosphoryl Lipid A adjuvant and Archimedes' chitosan (ChiSys) to enhance nasal delivery.

vernakalant

Cardiome, Astellas suspend patient enrollment in phase IIIb trial in atrial fibrillation

Cardiome announced on 21 October 2010 that its co-development partner Astellas has suspended enrollment in a multinational phase IIIb safety and efficacy trial, designated ACT 5, of iv vernakalant (KYNAPID) in patients with recent-onset symptomatic atrial fibrillation. This follows a single unexpected adverse event of cardiogenic shock in a patient who received vernakalant at a South American clinical site. The trial's Data Safety Monitoring Board has recommended continuation of the trial; however, the US FDA has requested to review all data relating to the adverse event in order to determine what steps, if any, are required before continuing the trial.

Vernakalant is a sodium and potassium channel blocker being developed as an iv and oral treatment for atrial fibrillation. The iv formulation of the product was granted marketing approval for this indication in the EU, Iceland and Norway in September 2010. A phase IIb trial of a controlled-release oral formulation of vernakalant is ongoing. Cardiome and Fujisawa (now known as Astellas) signed a licensing agreement in October 2003 to co-develop the compound as an iv formulation for the

See R&D Focus (Drug Updates) for full product details

treatment of atrial fibrillation and atrial flutter in North America. Merck & Co holds rights to iv vernakalant outside this region.

Conferences

AusBiotech 2010, 19-22 October 2010, Melbourne, Australia

Opportunities with Biota

BTA 798

Biota partnering opportunity, Worldwide

At AusBiotech 2010, 19-22 October 2010, Melbourne, Australia, Joy Hewitt, Director of Business Development at Biota, and Leigh Farrell, Vice President of Business Development, informed R&D Focus that BTA 798 is available for partnering, worldwide. BTA 798 is an orally acting antiviral that targets the rhinovirus capsid protein, for the prevention and treatment of rhinovirus infection in patients with compromised respiratory function due to asthma, chronic obstructive pulmonary disease (COPD) or cystic fibrosis. Phase IIb evaluation of BTA 798 in patients with chronic asthma is ongoing in the USA.

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FLUNET

Biota partnering opportunity, Worldwide

Biota and Daiichi Sankyo are developing FLUNET, an inhaled long acting neuraminidase (LANI) inhibitor, for the treatment and prevention of influenza A and B virus infections. The compounds are synthesized using Biota's FLUNET technology and are dimeric inhibitors based on the molecular shape of zanamivir. The therapy is intended to be a once-daily dosage for treatment and a once-weekly dosage for prevention. Preclinical studies are ongoing in Australia, supported by funding from the National Institute of Allergy and Infectious Diseases, an institute of the National Institutes of Health (NIH;USA). Joy Hewitt, Director of Business Development at Biota, and Leigh Farrell, Vice President of Business Development, informed R&D Focus at AusBiotech 2010, 19-22 October 2010, Melbourne, Australia, that FLUNET is available for partnering, worldwide.

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HCV infection therapy, Biota

Biota partnering opportunity, Worldwide

Biota is developing a small molecule non-nucleoside inhibitor for the treatment of hepatitis C virus (HCV) infection. Discovery stage research is ongoing in Australia. At AusBiotech 2010, 19-22 October 2010, Melbourne, Australia, Joy Hewitt, Director of Business Development at Biota, and Leigh Farrell, Vice President of Business

Development, informed R&D Focus that the HCV therapy program is available for licensing and/or partnering, worldwide.

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laninamivir

Biota partnering opportunity, Worldwide (excluding Japan)

Biota and Daiichi Sankyo are developing laninamivir (INAVIR), a long-acting neuraminidase inhibitor (LANI), for use by inhalation in the treatment and prophylaxis of influenza virus infections. In October 2010, Daiichi Sankyo launched laninamivir as a therapy for influenza virus infection in Japan. Phase I evaluation has been conducted in the UK. At AusBiotech 2010, 19-22 October 2010, Melbourne, Australia, Joy Hewitt, Director of Business Development at Biota, and Leigh Farrell, Vice President of Business Development, informed R&D Focus that laninamivir is available for licensing and/or partnering, worldwide, excluding Japan.

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RSV therapy, Biota

Biota partnering opportunity, Worldwide

In an interview at AusBiotech 2010, 19-22 October 2010, Melbourne, Australia, Joy Hewitt, Director of Business Development at Biota, and Leigh Farrell, Vice President of Business Development, provided an update on Biota's program to identify compounds for the treatment and prevention of respiratory syncytial virus (RSV) infection. Preclinical studies are ongoing in Australia and a lead compound has been nominated. Back up agents have also been developed. Biota is seeking partners for further development and funding of the program.

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BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan

Offers from GreenPeptide

vaccine, cervical cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

GreenPeptide is developing a vaccine for cervical cancer. The personalized immunotherapy, for patients with HLA

type A24, utilizes of a maximum of four peptide antigens selected from a group of 12, designated ITK-1. Translational clinical research, which predates preclinical studies, has been conducted in Japan. GreenPeptide is seeking partners for the further development of the vaccine. R&D Focus was informed of this opportunity at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, in an interview with Keizo Yoshida, Senior Adviser, Corporate Planning Division, GreenPeptide.

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vaccine, colorectal cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, that the company is seeking partners for the further development of its colorectal cancer vaccine. The personalized immunotherapy, for patients with HLA type A24, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-1. Translational clinical research, which predates preclinical studies, has been conducted in Japan.

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vaccine, HCV, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

GreenPeptide is developing a vaccine for the treatment of hepatitis C virus (HCV) infection. The personalized immunotherapy targets patients with HLA types A24, A2 or A3 and utilizes a maximum of four HCV peptide antigens selected from a group designated ITK-4. Pre-IND preclinical evaluation of the vaccine is being conducted in Japan. Keizo Yoshida, Senior Adviser, Corporate Planning Division, GreenPeptide, informed R&D Focus at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, that the HCV vaccine program is available for partnering, worldwide.

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vaccine, HLA-A2-positive glioblastoma multiforme, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

GreenPeptide is developing a vaccine for glioblastoma multiforme. The personalized immunotherapy, for patients with HLA type A2, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-2. Translational clinical research, which predates preclinical studies, has been conducted in Japan. The program is ready to enter preclinical studies when partnered. R&D Focus was informed that this vaccine program is available for worldwide partnering at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, in an interview with Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide.

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vaccine, HLA-A2-positive prostate cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, that the company's hormone-refractory prostate cancer vaccine program is available for worldwide partnering. The personalized immunotherapy, for patients with HLA type A2, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-2. Translational clinical research, which predates preclinical studies, has been conducted in Japan. The program is ready to enter preclinical studies when partnered.

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vaccine, HLA-A24-positive glioblastoma multiforme, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

GreenPeptide is developing a vaccine for malignant brain tumors. The personalized immunotherapy, for patients with HLA type A24, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-1. A phase I trial and phase IIa extension trial have completed in Japan in patients with glioblastoma multiforme. Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, that the company is seeking partners worldwide for the further development of its HLA-A24-positive glioblastoma multiforme vaccine. The program is ready to enter phase III when partnered.

See R&D Focus (Drug Updates) for full product details

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vaccine, HLA-A24-positive prostate cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

At BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus that the company's vaccine for HLA-A24-positive hormone-refractory prostate cancer (HRPC) is available for partnering, worldwide. The personalized immunotherapy utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-1. A phase I trial and phase IIa extension trial have completed in Japan in patients with HRPC, and GreenPeptide is planning to initiate phase III evaluation of the vaccine in 2011.

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vaccine, HLA-A3-positive solid tumors, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

GreenPeptide is developing a vaccine for solid tumors. The personalized immunotherapy, for patients with HLA type A3, utilizes a maximum of four peptide antigens selected from a group designated ITK-3. Translational clinical research, which predates preclinical studies, is under way in Japan. R&D Focus was informed that the program is available for worldwide partnering by Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, in an interview at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan.

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vaccine, lung cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

At BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus

that the company is seeking partners for the further development of its lung cancer vaccine. The personalized immunotherapy, for patients with HLA type A24, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-1. Translational clinical research, which predates preclinical studies, has been conducted in Japan.

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vaccine, pancreatic cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

GreenPeptide is developing a vaccine for pancreatic cancer. The personalized immunotherapy, for patients with HLA type A24, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-1. Translational clinical research, which predates preclinical studies, has been conducted in Japan. Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, that the company is seeking partners for the further development of the vaccine.

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vaccine, scirrhous gastric cancer, GreenPeptide

GreenPeptide partnering opportunity, Worldwide

Keizo Yoshida, Senior Adviser, Corporate Planning Division at GreenPeptide, informed R&D Focus at BioJapan 2010, 29 September-1 October 2010, Yokohama, Japan, that the company is seeking partners for the further development of its scirrhous gastric cancer vaccine. The personalized immunotherapy, for patients with HLA type A24, utilizes a maximum of four peptide antigens selected from a group of 12, designated ITK-1. Translational clinical research, which predates preclinical studies, has been conducted in Japan.

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BioPharm America, 15-17 September 2010, Boston, USA

Offers from AEterna Zentaris

AEZS 108

AEterna Zentaris partnering opportunity, Worldwide

AEterna Zentaris is developing AEZS 108, a cytotoxic conjugate comprising doxorubicin chemically linked to a luteinizing hormone-releasing hormone (LHRH) receptor agonist, for the treatment of LHRH receptor-positive tumors. A phase II trial has completed in the USA in ovarian and endometrial cancer patients. A phase II trial of the agent in patients with bladder cancer and a phase I/II trial in patients with castration- and taxane-resistant prostate cancer are expected to initiate in the USA before end 2010. At BioPharm America, 15-17 September 2010, Boston, USA, R&D Focus was informed by Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, that AEZS 108 is available for worldwide licensing and/or partnering.

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AEZS 112

AEterna Zentaris partnering opportunity, Worldwide

AEZS 112 is available for worldwide licensing and/or partnering, R&D Focus was informed by Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, at BioPharm America, 15-17 September 2010, Boston, USA. The agent, an oral, small molecule, dual tubulin and topoisomerase II inhibitor, is in phase I development for the treatment of lymphoma and solid tumors. An additional phase I trial is expected to initiate before end 2010.

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AEZS 115

AEterna Zentaris partnering opportunity, Worldwide

AEterna Zentaris is developing AEZS 115, the lead compound from a series of low molecular weight and orally bioavailable peptidomimetic luteinizing hormone releasing hormone (LHRH) antagonists. The agent has potential in the treatment of endometriosis, uterus myoma, benign prostatic hyperplasia, and cancers such as breast and prostate cancer. Preclinical studies are under way, and the agent is available for worldwide licensing and/or partnering. R&D Focus was informed of this opportunity in an interview with Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, at BioPharm America, 15-17 September 2010, Boston, USA.

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AEZS 120

AEterna Zentaris partnering opportunity, Worldwide

At BioPharm America, 15-17 September 2010, Boston, USA, R&D Focus was informed by Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, that AEZS 120 is available for worldwide licensing and/or partnering. The agent, a prostate cancer vaccine based on attenuated bacterial carriers, utilizes the immunogenicity and capacity of bacteria to colonize tumor tissues to deliver therapeutics such as prodrug-activating proteins. Phase I evaluation is expected to commence in early 2011.

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AEZS 123

AEterna Zentaris partnering opportunity, Worldwide

AEterna Zentaris is developing AEZS 123, a ghrelin receptor antagonist, for the treatment obesity and alcoholism. Preclinical evaluation is under way in Europe. At BioPharm America, 15-17 September 2010, Boston, USA, Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, informed R&D Focus that the agent is available for worldwide licensing and/or partnering.

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AEZS 127

AEterna Zentaris partnering opportunity, Worldwide

AEterna Zentaris is developing AEZS 127 (erucylphosphocholine), an analogue of the orally active alkylphosphocholine perifosine that is suitable for intravenous administration. The agent is a PI3K-Akt signal transduction inhibitor, and is undergoing preclinical development for the treatment of cancer. At BioPharm America, 15-17 September 2010, Boston, USA, R&D Focus was informed by Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, that AEZS 127 is available for worldwide licensing and/or partnering.

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See R&D Focus (Drug Updates) for full product details

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AEZS 129

AEterna Zentaris partnering opportunity, Worldwide

In an interview at BioPharm America, 15-17 September 2010, Boston, USA, Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, informed R&D Focus that the company is developing AEZS 129, an oral class I PI3K inhibitor, for the treatment of cancer. Preclinical studies are under way, and the agent is available for licensing and/or partnering, worldwide.

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AEZS 131

AEterna Zentaris partnering opportunity, Worldwide

Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, informed R&D Focus at BioPharm America, 15-17 September 2010, Boston, USA, that AEZS 131 is available for worldwide licensing and/or partnering. The agent, which has potential in the treatment of cancer, is a lead compound selected from a series of small molecules that inhibit ERK at nanomolar concentrations with good selectivity. Preclinical research is under way.

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AEZS 132

AEterna Zentaris partnering opportunity, Worldwide

At BioPharm America, 15-17 September 2010, Boston, USA, R&D Focus was informed by Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, that AEZS 132 is available for worldwide licensing and/or partnering. The agent, a pyridopyrazine dual inhibitor of PI 3-kinase and ERK, is in preclinical development for the treatment of cancer.

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disorazol E1

AEterna Zentaris partnering opportunity, Worldwide

Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris, informed R&D Focus at BioPharm America, 15-17 September 2010, Boston, USA, that disorazol E1 is available for worldwide licensing and/or partnering. The agent, a macrocyclic bislactone isolated from the myxobacterium Sorangium cellulosum, is undergoing preclinical studies as a potential treatment for cancer.

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perifosine

AEterna Zentaris partnering opportunity, Europe

Perifosine, an oral alkylphosphocholine, is available for licensing and/partnering in Europe. The agent inhibits Akt activation of the phosphoinositide 3-kinase (PI3K) pathway, and is under phase III evaluation in the treatment of multiple myeloma and colorectal cancer, and phase I and II evaluation in several other tumor types. R&D Focus was informed of this opportunity at BioPharm America, 15-17 September 2010, Boston, USA, by Eckhard Guenther, Vice President of Alliance Management & IP at AEterna Zentaris. The company also stated that it expects to expand the US phase III multiple myeloma trial to Europe before end 2010, and to report phase III data for perifosine by end 2011.

For further information on the opportunities available, contact:

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Opportunities with Biotecnol

CAB 051

Biotecnol partnering opportunity, Worldwide

At BioPharm America, 15-17 September 2010, Boston, USA, Pedro de Noronha Pissarra, CEO of Biotecnol, told R&D Focus that CAB 051, Biotecnol's fully human anti-HER2 antibody, is available for worldwide licensing and/or partnering. CAB 051, which targets the ErbB2 receptor, is undergoing preclinical evaluation for the treatment of gastric, prostate and bladder cancers. The antibody has shown significant anti-proliferative effects on tumor target cells and has demonstrated the ability to induce both antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. During preclinical in vivo tests, CAB 051 showed antineoplastic effects in HER2-positive tumors, including MUC4 overexpressing tumors, that do not respond to current anti-HER2 therapies. Synergistic effects with other anti-HER2 antibodies and anthracyclines have been observed. CAB 051 has a low cardiotoxicity and may be administered in patients presenting cardiotoxicity symptoms during treatment

See R&D Focus (Drug Updates) for full product details

with other anti-HER2 antibodies or anthracyclines.

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recombinant antibody derivative, breast cancer, Biotecnol

Biotecnol partnering opportunity, Worldwide

Biotecnol is developing a multifunctional recombinant antibody derivative that is active against four undisclosed targets. The agent, which was developed using the company's proprietary Tribody technology platform, has potential in the treatment of triple-negative breast cancer. Lead optimization studies are under way, and the program is available for licensing and/or partnering, worldwide. R&D Focus was informed of this opportunity at BioPharm America, 15-17 September 2010, Boston, USA, by Pedro de Noronha Pissarra, CEO of Biotecnol.

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recombinant antibody derivative, hematological cancer, Biotecnol

Biotecnol partnering opportunity, Worldwide

R&D Focus was informed during an interview at BioPharm America, 15-17 September 2010, Boston, USA, with Pedro de Noronha Pissarra, CEO of Biotecnol, that the company is developing a multifunctional recombinant antibody derivative that is active against CD19, CD20 and one undisclosed target. The agent, which was developed using the company's proprietary Tribody technology platform, has potential in the treatment of hematological cancer, including chronic lymphocytic leukemia (CLL), non-Hodgkin's lymphoma (NHL) and acute lymphoblastic leukemia (ALL). Lead optimization studies are under way, and the program is available for licensing and/or partnering, worldwide.

For further information on the opportunities available, contact:

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Tribody

Biotecnol licensing offer, Worldwide

Pedro de Noronha Pissarra, CEO of Biotecnol, informed R&D Focus at BioPharm America, 15-17 September 2010, Boston, USA, that the company's Tribody technology platform

is available for worldwide licensing. This drug design technology allows for the engineering of multifunctional recombinant antibody derivatives. The technology utilizes the natural in vivo heterodimerization of Fd fragments and light chains of an Fab fragment to form a scaffold upon which additional functions such as binders, cytokines, chemokines, growth factors, enzymes or protein toxins can be incorporated.

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BioPartnering Europe, 10-12 October 2010, London, UK

News from Circassia

ToleroMune

Circassia partnering opportunity, Worldwide

Circassia's ToleroMune technology platform for the development of vaccines against allergies is available for partnering, Charles Swingland, the company's Deputy Chairman, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK. The technology identifies short peptide T-cell epitope sequences (typically 10 to 20 amino acids) from proteins. The peptides are selected for their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells. ToleroMune selects an optimal peptide mixture to ensure broad population coverage across the multiple different MHC class II alleles. Administration of the T-cell epitopes activates regulatory T cells that downregulate an allergic response to the allergens from which epitopes were derived; this leads to the development of tolerance to the allergen. Peptides selected by ToleroMune are linear so do not contain the B-cell epitopes that are present in whole allergen; these can cause cross-linking of IgE on the surface of mast cells, which is associated with itchy eyes, runny nose and asthmatic responses on exposure to allergen, and anaphylactic type reactions. Circassia is using ToleroMune to develop vaccines to a range of allergens, including ragweed, grass and cat allergies, and for the prevention of transplant rejection and rheumatoid arthritis.

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vaccine, Alternaria allergy, Circassia

Circassia partnering opportunity, Worldwide

Circassia is developing a vaccine for the treatment of Alternaria allergy. The vaccine, which is based on the use of small peptide T-cell epitopes derived from Alternaria allergens, was generated using the company's ToleroMune technology which identifies short peptide sequences (typically 10 to 20 amino acids) from proteins. The peptides are selected for their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells. Preclinical studies are under way in the UK. At

BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the Alternaria allergy vaccine is available for partnering, worldwide, as part of a package with other allergy vaccines in the company's pipeline.

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vaccine, birch pollen allergy, Circassia

Circassia partnering opportunity, Worldwide

At BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the company's birch pollen allergy vaccine is available for partnering, worldwide, as part of a package with other allergy vaccines in the company's pipeline. Preclinical studies of the vaccine are ongoing.

The birch pollen allergy vaccine is based on the use of small peptide T-cell epitopes derived from birch pollen allergens. The vaccine was generated using the company's ToleroMune technology, which identifies short peptide sequences (typically 10 to 20 amino acids) from proteins. The peptides are selected for their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells.

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vaccine, cat allergy, Circassia

Circassia partnering opportunity, Worldwide

Circassia is developing a vaccine for cat allergy based on seven specific T-cell epitopes derived from cat dander, generated using the company's ToleroMune technology. ToleroMune technology identifies short peptide sequences from proteins, which are then selected based on their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells. ToleroMune technology selects an optimal peptide mixture to ensure broad population coverage across the multiple different MHC class II alleles. The vaccine is under phase II evaluation in Canada, with phase III trials expected to start in 2011. At BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the cat allergy vaccine is available for partnering, worldwide, as part of a package with other allergy vaccines in the company's pipeline.

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vaccine, grass allergy, Circassia

Circassia partnering opportunity, Worldwide

Circassia is developing a vaccine for grass allergy, based on the use of small peptide T-cell epitopes derived from grass allergens. The vaccine was generated using the company's ToleroMune technology, which identifies short peptide sequences (typically 10 to 20 amino acids) from proteins. The peptides are selected for their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells. A phase II trial of the vaccine started in Canada in September 2010. At BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the grass allergy vaccine is available for partnering, worldwide, as part of a package with other allergy vaccines in the company's pipeline.

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vaccine, house dust mite allergy, Circassia

Circassia partnering opportunity, Worldwide

At BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the company's house dust mite allergy vaccine is available for partnering, worldwide, as part of a package with other allergy vaccines in the company's pipeline. The vaccine is based on the use of small peptide T-cell epitopes derived from house dust mite allergens. The vaccine was generated using the company's ToleroMune technology, which identifies short peptide sequences (typically 10 to 20 amino acids) from proteins. The peptides are selected for their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells. A phase II trial of the vaccine initiated in Canada in January 2010; phase II evaluation is expected to complete fourth quarter 2011, with phase III trials expected to start in 2012.

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vaccine, Japanese cedar allergy, Circassia

Circassia partnering opportunity, Worldwide

Circassia is developing a vaccine for the treatment of Japanese cedar allergy. The vaccine is based on the use of small peptide T-cell epitopes derived from the Japanese cedar. It was generated using the company's ToleroMune technology, which identifies short peptide sequences (typically 10 to 20 amino acids) from proteins. The peptides are selected for their ability to bind to multiple MHC Class II molecules on the surface of antigen presenting cells. Preclinical studies are under way in the UK. At

See R&D Focus (Drug Updates) for full product details

BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the Japanese cedar allergy vaccine is available for partnering, worldwide, either on its own or as part of a package with other allergy vaccines in the company's pipeline.

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vaccine, ragweed allergy, Circassia

Circassia partnering opportunity, Worldwide

At BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the company's ragweed allergy vaccine is available for partnering, worldwide, as part of a package including other allergy vaccines in the company's pipeline. Phase II evaluation of the vaccine is ongoing in Canada in patients with allergic rhinoconjunctivitis caused by exposure to ragweed. Phase II evaluation of the ragweed allergy vaccine is expected to complete in 2011, with phase III evaluation anticipated to start second half 2011 or first half 2012.

The ragweed allergy vaccine was developed using Circassia's proprietary ToleroMune technology, which identifies and utilizes antigen epitopes to generate regulatory T cells that reduce immune responses.

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vaccine, rheumatoid arthritis, Circassia

Circassia conducting discovery program

At BioPartnering Europe, 10-12 October 2010, London, UK, Charles Swingland, Deputy Chairman at Circassia, informed R&D Focus that the company is developing a vaccine for the treatment of rheumatoid arthritis. The vaccine is based on the use of small peptide T-cell epitopes derived from proteins involved in the pathogenesis of the disease. The vaccine was generated using the company's ToleroMune technology, which identifies short peptide sequences (typically 10 to 20 amino acids) from proteins. The program is being conducted in collaboration with McMaster University (Canada); discovery stage research is under way.

Offers from Victory Pharma

MGX 001

Victory Pharma licensing offer, Worldwide

MGX 001 is available for licensing, worldwide, David Tomasso, Executive Director of Business Development at Victory Pharma, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK. MGX 001 is a fixed combination of a marketed product and morphine, under development for the treatment of chronic severe pain without the side effects of opiate-induced therapy. A randomized, double-blind, placebo-controlled, crossover,

phase II trial has been completed in the USA. The study has provided guidance regarding dose ranging and proof of concept for MGX 001.

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MOXATAG

Victory Pharma licensing offer, Worldwide (excluding USA)

At BioPartnering Europe, 10-12 October 2010, London, UK, David Tomasso, Executive Director of Business Development at Victory Pharma, informed R&D Focus that MOXATAG is available for licensing, worldwide excluding the USA. MOXATAG utilizes the company's once-a-day pulsatile delivery technology, PULSYS, to deliver amoxicillin at lower dosages over a shorter duration of therapy. In March 2009, MOXATAG was launched in the USA for the treatment of pharyngitis/tonsillitis secondary to Streptococcus pyogenes infection in adults and children aged 12 years and older. Victory Pharma acquired the assets of Middlebrook, including MOXATAG, in August 2010.

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PULSYS

Victory Pharma licensing offer, Worldwide

Victory Pharma's PULSYS drug delivery technology is available for licensing, worldwide, David Tomasso, Executive Director of Business Development at Victory Pharma, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK. PULSYS enables oral once-daily pulsatile delivery of molecules. The technology covers antibiotics, alone or in combination, antifungals, alone or in combination, antivirals and antineoplastics. The technology was originally developed by Advancis, which changed its name to Middlebrook in June 2007; Middlebrook sold this asset to Victory Pharma in August 2010.

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See R&D Focus (Drug Updates) for full product details

Opportunities with Italfarmaco

givinostat

Italfarmaco partnering opportunity, USA

At BioPartnering Europe, 10-12 October 2010, London, UK, Elisabetta Capezio, Licensing Manager at Italfarmaco, informed R&D Focus that givinostat (ITF 2357) is available for partnering in the USA. The agent, a histone deacetylase (HDAC) inhibitor, is being developed for the treatment of inflammatory diseases and cancer. Phase II trials of givinostat in the treatment of juvenile arthritis, myeloproliferative diseases, Hodgkin's lymphoma and multiple myeloma have been conducted. Phase III trials in patients with myeloproliferative diseases and juvenile arthritis are expected to start first quarter 2011.

For further information on the opportunities available, contact:

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ITF 2534

Italfarmaco partnering opportunity, Worldwide

At BioPartnering Europe, 10-12 October 2010, London, UK, R&D Focus was informed by Elisabetta Capezio, Licensing Manager at Italfarmaco, that ITF 2534 is available for partnering, worldwide. The agent, a triazole enantiomer, is being developed as a therapy for fungal infections. ITF 2534 has been evaluated in a phase I trial.

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Opportunities with Proacta

HSMKI technology platform

Proacta partnering opportunity, Worldwide

Proacta's HSMKI (hypoxia-selective multi-kinase inhibitor) technology platform allows the development of small molecule prodrugs that become active in the presence of tumor hypoxia. The technology is based on a hypoxia-selective trigger which is attached to the tyrosine kinase inhibitor. Oxygen prevents the trigger from separating and a positive charge on the trigger limits the entry of the HSMKI complex into the cells. In the absence of oxygen, the trigger separates from the inhibitor which can then enter cells. Proacta's HSMKI technology platform is available for partnering, worldwide, for the co-development of new cancer therapies or the improvement of existing therapies, Seth Goldblum, a representative for Proacta, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK.

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PR 104

Proacta licensing offer, Worldwide

A phase I/II trial of PR 104 started in the USA in patients with refractory/relapsed acute myelogenous leukemia (AML) in first quarter 2010, Seth Goldblum, a representative for Proacta, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK. As of 1 September 2010, 14 patients were enrolled in the study. Complete response (CR and CRp) on day 42 is the primary efficacy endpoint of the trial. Final results are expected in first quarter 2011. PR 104 is being developed for the treatment of cancer, with an initial focus on AML. The agent is converted to a DNA damaging compound, PR 104A, in hypoxic regions in tumors. A phase II trial of PR 104 has been conducted in small cell lung cancer. PR 104 is available for licensing, worldwide.

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hypoxia-activated kinase inhibitors, Proacta

Proacta preclinical evaluation, USA (solid tumor)

Proacta is developing hypoxia-activated protein kinase inhibitors for the treatment of solid tumors. The agents have been designed using Proacta's HSMKI (hypoxia-selective multi-kinase inhibitor) technology platform which allows for the development of small molecule prodrugs that become active in the presence of tumor hypoxia. The technology is based on a hypoxia selective trigger which is attached to the tyrosine kinase inhibitor (the effector). Oxygen prevents the trigger from separating and a positive charge on the trigger limits the entry of the HSMKI complex into the cells. In the absence of oxygen, the trigger separates from the inhibitor which can then enter into cells. A series of effectors and trigger combinations are being evaluated; three prodrugs have been identified from an initial screen of 15. Preclinical studies are ongoing in the USA. Seth Goldblum, a representative of Proacta, informed R&D Focus of the status of this program at BioPartnering Europe, 10-12 October 2010, London, UK.

PR 509

Proacta licensing offer, Worldwide

At BioPartnering Europe, 10-12 October 2010, London, UK, Seth Goldblum, a representative of Proacta informed R&D Focus that the company is developing PR 509, a hypoxia-activated irreversible pan-erbB inhibitor, for the treatment of erlotinib-resistant nonsmall cell lung cancer (NSCLC). The agent has been designed using Proacta's HSMKI (hypoxia-selective multi-kinase inhibitor) technology platform which allows the development of small molecule prodrugs that become active in the presence of tumor hypoxia. The technology is based on a hypoxia-selective trigger which is attached to the tyrosine kinase inhibitor. Oxygen prevents the trigger from separating and a positive charge on the trigger limits the entry of the HSMKI complex into the cells. In the absence of oxygen, the trigger separates from the inhibitor which can then enter cells. Preclinical studies of PR 509 are ongoing in the USA. The pan-erbB inhibitor contained in PR 509 was active in erlotinib-resistant tumors with the T790M mutation. The agent showed greater activity than other irreversible pan-erbB inhibitors in development such as BIBW 2992 or HKI 272. The agent had a long half-life in tumors. PR 509 was more active than erlotinib in A431 xenograft models and superior to BIBW 2992 in H1975 xenograft models. PR 509 was orally active at less than 25% of the maximum tolerated dose in A431 xenograft models. Pre-IND studies are expected to start in November 2010. PR 509 is available for licensing, worldwide.

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Company Focus

Focus on Mind-NRG

Mind-NRG was founded in October 2010 and is based in Switzerland. The company is developing disease modifying agents, including NRG 101, which show potential in the treatment of neurological and psychiatric disorders.

NRG 101

Mind-NRG developing therapy for CNS disorders

Mind-NRG is developing NRG 101, a peptide neurotrophic factor with potential in the treatment of CNS disorders, including Alzheimer's disease, Parkinson's disease and schizophrenia. The peptide crosses the blood-brain barrier by a receptor-mediated transport and shows disease-modifying potential. NRG 101 improved cognition and restored neural architecture in relevant preclinical models of neurodegeneration. Preclinical mechanism of action studies in vitro and in vivo, and studies utilizing relevant disease models, are ongoing in Switzerland. Mind-NRG has secured up to EUR10 million in Series A financing to fund preclinical development of NRG 101.

Focus on Reviva

Reviva was founded in 2006 and is located in San Jose (California, USA). The pharmaceutical company is developing a portfolio of internally discovered new chemical entities using its integrated chemical genomics-based technology platform and proprietary chemistries. Reviva is currently focusing on developing drugs for CNS disorders, cardiovascular diseases, metabolic and inflammatory indications.

RP 1000

Reviva is planning an IND submission

Vinay Chhatre, Director of Business Development and Strategic Alliances at Reviva, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK, that the company is developing RP 1000 for the oral treatment of obesity. The company is using an integrated chemical genomics-based technology platform and proprietary chemistries for the discovery of new chemical entities (NCE). Discovery stage research is ongoing in the USA. Reviva is planning to select a preclinical candidate in December 2010 and to submit an IND application to the US FDA in March or April 2011.

RP 3000

Reviva conducting discovery program, USA (GERD)

Reviva is developing RP 3000 for the oral treatment of gastroesophageal reflux disease (GERD), using an integrated chemical genomics-based technology platform and proprietary chemistries for the discovery of new chemical entities (NCE). Discovery stage research is ongoing in the USA, Vinay Chhatre, Director of Business Development and Strategic Alliances at Reviva, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK.

RP 4000

Reviva conducting discovery program, USA (Alzheimer's disease)

At BioPartnering Europe, 10-12 October 2010, London, UK, Vinay Chhatre, Director of Business Development and Strategic Alliances at Reviva, informed R&D Focus that the company is developing RP 4000 for the oral treatment of

Alzheimer's disease, using an integrated chemical genomics-based technology platform and proprietary chemistries. Discovery stage research is ongoing in the USA.

RP 5000

Reviva IND submission, USA (schizophrenia)

Reviva licensing offer, Worldwide

Reviva submitted an IND application to the US FDA in October 2010 for the initiation of a phase I trial of RP 5000, Vinay Chhatre, Director of Business Development and Strategic Alliances at Reviva, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK. RP 5000 is a new chemical entity (NCE) in development for the oral treatment of schizophrenia. The phase I trial is scheduled to start in early December 2010. The agent is available for out-licensing, worldwide.

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RP 6000

Reviva conducting discovery program, USA (depression)

Using an integrated chemical genomics-based technology platform and proprietary chemistries, Reviva is developing RP 6000 for the oral treatment of depression. Discovery stage research is ongoing in the USA, Vinay Chhatre, Director of Business Development and Strategic Alliances at Reviva, informed R&D Focus at BioPartnering Europe, 10-12 October 2010, London, UK.

Newly Reported Drugs in R&D Focus				
Company	**Product**	**Therapeutic Class***	**Indication**	**Phase**
AEterna Zentaris	AEZS 129	L1X9	cancer	Preclinical
ASKA	AKP 002	L1X9	benign prostatic hyperplasia	Phase I
Biotecnol	recombinant antibody derivative, breast cancer, Biotecnol	L1X9	breast cancer	Discovery
Biotecnol	recombinant antibody derivative, hematological cancer, Biotecnol	L1X9	hematological cancer	Discovery
Cancer Research Technology	drug design technology, DNA fusion vaccines, Cancer Research Technology	V7A	Drug Design Technology	Technology
Cancer Research Technology	target, CLEC9A, Cancer Research Technology	J7C	cancer; infectious disease	Discovery
Circassia	vaccine, Alternaria allergy, Circassia	J7C; V1A	allergy	Preclinical
Circassia	vaccine, Japanese cedar allergy, Circassia	J7C; V1A	allergy	Preclinical
Circassia	vaccine, rheumatoid arthritis, Circassia	J7C; M1C	rheumatoid arthritis	Discovery
Cytos	vaccine, malaria, Cytos/NIH	J7A9	malaria	Discovery
GlaxoSmithKline	gene therapy, ADA-SCID, GlaxoSmithKline	V3X	genetic disorder	Phase I/II
GlaxoSmithKline	gene therapy, beta-thalassemia, GlaxoSmithKline/ Telethon/San Raffaele Del Monte Tabor Foundation	B3X	thalassemia	Preclinical
GlaxoSmithKline	gene therapy, CGD, GlaxoSmithKline/Telethon/San Raffaele Del Monte Tabor Foundation	V3X	genetic disorder	Preclinical
GlaxoSmithKline	gene therapy, GLD, GlaxoSmithKline/Telethon/San Raffaele Del Monte Tabor Foundation	V3X	lysosomal storage disorder	Preclinical
GlaxoSmithKline	gene therapy, MLD, GlaxoSmithKline/Telethon/San Raffaele Del Monte Tabor Foundation	N7X	lysosomal storage disorder	Phase I/II
GlaxoSmithKline	gene therapy, MPS, GlaxoSmithKline/Telethon/San Raffaele Del Monte Tabor Foundation	V3X	mucopolysaccharidosis	Preclinical
GreenPeptide	vaccine, HLA-A3-positive solid tumors, GreenPeptide	J7C; L3A9	solid tumor	Discovery
Lumiphore	Lumi4 complexes	V7A	Drug Design Technology	Technology
MacroGenics	DART protein, cancer, MacroGenics/Pfizer	L1X9	cancer	Discovery
Merck Serono	drug delivery system, MEDUSA extended-release interferon beta-1a, Merck Serono/Flamel Technologies	V3X; V7A	all other therapeutics	Clinicals
Mind-NRG	NRG 101	N4A; N5A1; N7D9	Alzheimer's disease; Parkinson's disease; schizophrenia	Preclinical

Newly Reported Drugs in R&D Focus				
Company	**Product**	**Therapeutic Class***	**Indication**	**Phase**
Proacta	HSMKI technology platform	V7A	Drug Design Technology	Technology
Proacta	hypoxia-activated kinase inhibitors, Proacta	L1X4; V7A	solid tumor	Preclinical
Proacta	PR 509	L1X4; V7A	NSCLC	Preclinical
Reviva	RP 1000	A8A	obesity	Discovery
Reviva	RP 3000	A16A	GERD	Discovery
Reviva	RP 4000	N7D9	Alzheimer's disease	Discovery
Reviva	RP 5000	N5A1	schizophrenia	Preclinical
Reviva	RP 6000	N6A2	depression	Discovery
Sanofi Pasteur	FLUZONE Quadrivalent	J7A1	influenza	Phase II
Stanford University	18F-FPPRGD2	T1X	diagnosis	Clinicals
to-BBB	drug delivery system, stroke therapy, NeuroVive/to-BBB	N7X	stroke	Discovery

*** A change in phase may not apply to all therapeutic classes and indications**

See R&D Focus (Drug Updates) for full product details

Product Phase Changes Reported in R&D Focus						
Company	**Product**	**Therapeutic Class***	**Indication**	**NewPhase**	**Region of Phase Change**	**Highest Phase**
AstraZeneca	CytoFab	V3X	sepsis; septic shock	Phase II	Worldwide	Phase II
Baxter	GLASSIA	R7X	enzyme deficiency	Marketed	USA	Marketed
Calistoga	CAL 101	L1X9	CLL; lymphoma	Phase II	USA	Phase II
Cytheris	CYT 107	J5B1; J5C9; L3A9	HIV infection	Phase II	France; Italy; Spain; UK	Phase II
ImmuneWorks	IW 001	R7X	pulmonary fibrosis	Phase I	USA	Phase I
Lilly	prasugrel	B1C2	acute coronary syndrome	Marketed	India	Marketed
Meda	BEMA fentanyl	N2A; V7A	pain	Registered	EU	Marketed
MolMed	NGR-hTNF	L1X9	soft tissue sarcoma	Phase II	Italy	Phase III
PTC Therapeutics	ataluren	B6C; M5X; R7X	metabolic disease	Phase II	Europe	Phase III
Repros Therapeutics	enclomifene	A10X9; G3B	diabetes	Phase II	USA	Phase III
Roche	trastuzumab	L1X3	gastric cancer	Marketed	USA	Marketed
sanofi-aventis	teriflunomide	N7X	multiple sclerosis	Phase III	Worldwide	Phase III
Shionogi	GSK 1349572	J5C9	HIV infection	Phase III	Europe; USA	Phase III
Tibotec Pharmaceuticals	telaprevir	J5B1	hepatitis C	Phase III	Worldwide	Pre-registration
ViiV Healthcare	GSK 1349572	J5C9	HIV infection	Phase III	Europe; USA	Phase III

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