

BioCentury Part II

ESSENTIAL SURVEILLANCE FOR BIOTECH & PHARMA

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BioBusiness for the week ended August 6

COMPANY NEWS

Deals (Page B2)

Altair/Cornerstone (NASDAQ:CRTX)
 Amplimmune/GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 Anacor/GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 Axiogenesis/Kyoto U
 Biovail (TSX:BVF; NYSE:BVF)/Lambda Therap
 BrainCells/Proximagen (LSE:PRX)
 Celera (NASDAQ:CRA)/Ipsen (Euronext:IPN)
 Cornerstone (NASDAQ:CRTX)/Targacept (NASDAQ:TRGT)
 CyDex/U of Kansas
 Cypress (NASDAQ:CYPB)
 Evotec (Xetra:EVT)/Boehringer Ingelheim
 Five Prime Therap/GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 Forbes Medi-Tech (OTCBB:FMTI)/Marco Hi-Tech
 FTA Bio/Pure Bio (NASDAQ:PURE)
 Galapagos (Euronext:GLPG; Pink:GLPYY)/GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 GenSpera (OTCBB:GNSZ)/Johns Hopkins U/ U of Copenhagen
 Lexicon (NASDAQ:LXRX)/Symphony Icon
 Middlebrook (PINK:MBRKQ)/Victory Pharma
 MorphoSys (Xetra:MOR)/U College London
 Movetis (Euronext:MOVE)/Shire (LSE:SHP; NASDAQ:SHPGY)
 Osteologix (OTCBB:OLGX)/Servier
 Hard to Treat Diseases (Pink:HTDS)
 Radient (NYSE-A:RPC)/Shanxi
 Seattle Genetics (NASDAQ:SGEN)/Roche (SIX:ROG; OTCQX:RHHBY)
 TapImmune (OTCBB:TPIV)/Mayo Clinic
 Vectura (LSE:VEC)/GlaxoSmithKline (LSE:GSK; NYSE:GSK)

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Celera (NASDAQ:CRA)

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Alcon (NYSE:ACL)/Nestle (SIX:NESN)/Novartis (NYSE:NVS; SIX:NOVN)
 Cleveland BioLabs (NASDAQ:CBLI)/U.S. Dept of HHS

Using BioCentury Part II

BioCentury Part II is a comprehensive compendium of business news for management and investors in bioscience companies. It is organized into three departments: Company News, Clinical News and Financial News.

The index on this page lists all the companies covered this week. The news items in each department are organized alphabetically by company. When more than one company is listed, the biotech company is shown first. Each brief is labeled with one or more applicable business categories from the following list:

ADMET; Agbio/Environmental; Antibodies; Autoimmune; Bioinformatics; Biomanufacturing; Biopharmaceuticals; Biosimilars; Cancer; Cardiovascular; Chemistry; Combinatorial biology; Computational chemistry/biology; Dental; Dermatology; Diagnostic; Drug delivery; Endocrine; Finance; Functional genomics; Gastrointestinal; Gene/Cell therapy; Generics; Genitourinary; Genomics; Hematology; Hepatic; High throughput screening; Infectious; Inflammation; Metabolic; Microarrays; Microfluidics; Musculoskeletal; Neurology; Nutraceuticals; Ophthalmic; Other; Pharmaceuticals; Pharmacogenetics; Proteomics; Pulmonary; Renal; Supply/Service; Transplant; Veterinary

Cypress (NASDAQ:CYPB)/Forest (NYSE:FRX)
 Elusys Therap/U.S. Dept of HHS
 Genzyme (NASDAQ:GENZ)/U.S. Dept of HHS
 Lpath (OTCBB:LPTN)
 Medicines Co. (NASDAQ:MDCO)
 NicOx (Euronext:COX)
 Pfenex
 Servier
 Vectura (LSE:VEC)

Management Tracks (Page B7)

Aragon Pharma
 AstraZeneca (LSE:AZN; NYSE:AZN)
 BioAlliance (Euronext:BIO)

CT Atlantic
 Formac Pharma
 Living Cell Tech (ASX:LCT; OTCQX:LVCLY)
 Lupin (NSE:LUPIN; BSE:500257)
 Nycomed
 Penwest (NASDAQ:PPCO)
 PharmaGap (TSX-V:GAP)
 Pharminox
 Photocure (OSE:PHO)
 Signum Bio
 Tengion (NASDAQ:TNGN)
 Tolerx

CLINICAL NEWS

Regulatory (Page B8)

Abbott (NYSE:ABT)
 Abraxis (NASDAQ:ABII)/Otsuka (Tokyo:4768)
 Accelaron
 Acrux (ASX:ACR)/Vivus (NASDAQ:VVUS)
 AdvanDx
 Affymax (NASDAQ:AFFY)/Takeda (Tokyo:4502)
 Allergan (NYSE:AGN)
 Allergan (NYSE:AGN)/GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 Arena (NASDAQ:ARNA)
 Astellas (Tokyo:4503)
 Bayer (Xetra:BAY)
 Boehringer Ingelheim/Bristol-Myers (NYSE:BMJ)/sanofi-aventis (Euronext:SAN; NYSE:SNY)
 Celldex (NASDAQ:CLDX)
 CSL (ASX:CSL)
 Dendreon (NASDAQ:DNDN)
 Devax
 GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 Isotechnika (TSX:ISA)/Lux
 Jazz (NASDAQ:JAZZ)
 Merz
 Movetis (Euronext:MOVE)/J&J (NYSE:JNJ)
 Progenics (NASDAQ:PGNX)/Ono (Tokyo:4528; Osaka:4528)/Pfizer (NYSE:PFE)
 sanofi-aventis (Euronext:SAN; NYSE:SNY)
 Shire (LSE:SHP; NASDAQ:SHPGY)/Dainippon Sumitomo (Tokyo:4506; Osaka:4506)
 Xoma (NASDAQ:XOMA)

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COMPANY NEWS/Deals, Sales & Marketing, Other News, Management Tracks

DEALS

Alitair Pharmaceuticals Inc., Morris Plains, N.J.
Cornerstone Therapeutics Inc. (NASDAQ:CRTX), Cary, N.C.
 Business: Pulmonary, Infectious

Alitair granted Cornerstone a license to its IP covering solid oral dosage formulations, which the companies will use to collaborate on the development of one or more compounds to treat cough and cold. The license will be exclusive as long as the companies continue to actively collaborate. Alitair will receive an upfront payment and will be eligible for milestones and royalties. Additional financial terms were not disclosed.

Amplimmune Inc., Rockville, Md.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
 Business: Cancer, Infectious

Amplimmune granted GlaxoSmithKline an exclusive, worldwide license to develop and commercialize AMP-224 and other next-generation fusion proteins targeting PD-1 receptor (PDCD1; PD-1; CD279). Amplimmune will receive \$23 million up front and is eligible to receive up to \$485 million in milestones, plus double-digit royalties. Amplimmune is responsible for preclinical testing and a single Phase I trial of AMP-224 to treat cancer, which is slated to start next year. AMP-224 is also in preclinical development to treat infectious disease. GSK is responsible for all further manufacturing, development and commercialization.

AMP-224 is a fusion protein that blocks the interaction between PD-1 and programmed cell death 1 ligand 1 (CD274 molecule; PD-L1; B7-H1).

Anacor Pharmaceuticals Inc., Palo Alto, Calif.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
 Business: Infectious

GlaxoSmithKline exercised an option to license exclusive, worldwide rights from Anacor to develop and commercialize GSK2251052 (formerly AN3365), a boron-based, small-molecule antibiotic targeting the bacterial enzyme leucyl-tRNA synthetase (LARS; LeuRS). GSK received the option under a 2007 deal granting the pharma an exclusive option to license worldwide rights to at least eight boron-containing small molecules against up to four targets to treat viral and bacterial diseases. The companies reported Phase I data in June for GSK2251052 in Gram-negative bacterial infections. Anacor will receive a \$15 million option exercise fee and is eligible for \$84 million in milestones, plus tiered, double-digit royalties up to the mid-teens (see *BioCentury*, Oct. 15, 2007 & July 12, 2010).

Axiogenesis AG, Cologne, Germany
Kyoto University, Kyoto, Japan
 Business: Gene/Cell therapy

Axiogenesis received a non-exclusive, worldwide license to an induced pluripotent stem (iPS) cell patent portfolio from the university's

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Clinical News, from previous page

Clinical Results (Page B11)

Bayer (Xetra:BAY)/J&J (NYSE:JNJ)
 BioMarin (NASDAQ:BMRN)/Merck KGaA (Xetra:MRK)
 BioMarin (NASDAQ:BMRN)/Summit (LSE:SUMM)
 Cardioxyl
 Excaliard/Isis (NASDAQ:ISIS)
 Ganymed
 Genzyme (NASDAQ:GENZ)/Isis (NASDAQ:ISIS)
 Hopital Necker-Enfants Malades
 Infinity (NASDAQ:INFI)
 Innocoll
 Merck (NYSE:MRK)
 Northwest (OTCBB:NWBO)
 Oncimmune/Proteome (LSE:PRM)
 Vicept
 YM BioSci (TSX:YM; NYSE-A:YMI)

Preclinical Results (Page B15)

Argos
 DiaMedica (TSX-V:DMA)
 FTA Bioscience/Pure (NASDAQ:PURE)
 GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 PharmaGap (TSX-V:GAP)
 Virxsys

Clinical Status (Page B16)

Acceleron/Celgene (NASDAQ:CELG)
 Access (OTCBB:ACCP)
 Aeterna (TSX:AEZ; NASDAQ:AEZS)
 Astellas (Tokyo:4503)
 Bio-Path (Pink:BPTH)
 Biovail (TSX:BVF; NYSE:BVF)
 Boston Scientific (NYSE:BSX)
 Celgene (NASDAQ:CELG)
 Cell Therap (NASDAQ:CTIC; Milan:CTIC)
 Celldex (NASDAQ:CLDX)
 Galapagos (Euronext:GLPG; Pink:GLPYY)
 Living Cell (ASX:LCT; OTCQX:LVCLY)
 N30 Pharma
 Neurocrine (NASDAQ:NBIX)/GlaxoSmithKline (LSE:GSK; NYSE:GSK)
 Novartis (NYSE:NVS; SIX:NOVN)
 Patrys (ASX:PAB)
 Pozen (NASDAQ:POZN)
 UCB (Euronext:UCB)
 ZymoGenetics (NASDAQ:ZGEN)

Bradmer (TSX:BMR)
 Gemin X
 Helix (TSX:HBP; Xetra:HBP)
 Idera (NASDAQ:IDRA)
 NuPathe (NASDAQ:PATH)
 Sareum (LSE:SAR)
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 Wilex (Xetra:WL6)

Proposed Offerings (Page B19)

Arena (NASDAQ:ARNA)
 Biofrontera (Xetra:B8F)
 Biohit (HSE:BIOBV)
 Complete Genomics
 Horizon Pharma

Other Financial News (Page B20)

Aradigm (OTCBB:ARDM)
 Cardioxyl
 Genta (OTCBB:GETAD)
 KV Pharma (NYSE:KVA)
 Marina Bio (NASDAQ:MRNAD)
 Molecular Insight (NASDAQ:MIPI)
 MolMed (Milan:MLM)
 Neoprobe (OTCBB:NEOP)
 Patrys (ASX:PAB)
 PDL (NASDAQ:PDLI)
 PharmAthene (NYSE-A:PIP)

FINANCIAL NEWS

Completed Offerings (Page B19)

Alexza (NASDAQ:ALXA)

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technology transfer arm, iPS Academia Japan Inc. Further terms were not disclosed.

Biovail Corp. (TSX:BVF; NYSE:BVF), Mississauga, Ontario
Lambda Therapeutic Research Ltd., Ahmedabad, India
Business: Supply/Service

Biovail disclosed in its 2Q10 earnings that on July 23 it completed the sale of its contract research division to Lambda for \$6 million in cash. Biovail said the division no longer fit its core focus on CNS. In 2009, Biovail's R&D revenues were \$14.1 million, including the CRO unit, and said that after the sale R&D revenues would be "inconsequential." Avendus Capital Pvt. Ltd. advised Lambda and Fairmount Partners advised Biovail. Biovail is merging with Valeant Pharmaceuticals International (NYSE:VRX, Aliso Viejo, Calif.) (see *BioCentury*, June 28).

BrainCells Inc., San Diego, Calif.
Proximagen Group plc (LSE:PRX), London, U.K.
Business: Neurology

BrainCells will acquire exclusive, worldwide rights to develop and commercialize Proximagen's sabcomeline. The selective muscarinic acetylcholine receptor M1 (CHRM1; HMI) partial agonist is in Phase II testing to treat schizophrenia. BrainCells is responsible for developing and marketing sabcomeline, for which BrainCells expects to start Phase II testing to treat major depressive disorder (MDD) next year. Proximagen is eligible to receive up to \$51 million in an upfront payment and milestones, plus royalties. Further financial terms were not disclosed.

Proximagen gained rights to sabcomeline through its acquisition of Minster Pharmaceuticals plc this year. Minster had rights to sabcomeline from GlaxoSmithKline plc (LSE:GSK; NYSE:GSK, London, U.K.) (see *BioCentury*, Jan. 11).

Celera Corp. (NASDAQ:CRA), Alameda Calif.
Ipsen Group (Euronext:IPN), Paris, France
Business: Diagnostic

Celera disclosed in its 2Q10 earnings that in June it extended a 2007 deal with Ipsen to discover and characterize biomarkers for growth failure. Further financial terms were not disclosed (see *BioCentury*, Dec. 3, 2007).

Cornerstone Therapeutics Inc. (NASDAQ:CRTX), Cary, N.C.
Targacept Inc. (NASDAQ:TRGT), Winston-Salem, N.C.
Business: Pharmaceuticals

Cornerstone granted Targacept exclusive, worldwide rights to its nicotinic receptor patents and preclinical compounds that target the receptors, including nicotinic acetylcholine receptor alpha 7 (CHRNA7). Cornerstone will receive \$1.5 million up front and is eligible for milestones, plus low single-digit royalties. The exact amount of milestone payments depends on which of two compounds Targacept moves into clinical trials. Cornerstone is eligible for \$1.1-\$1.4 million in milestones through Phase II proof of concept (POC) testing, \$9.5-\$18.5 in additional pre-commercialization milestones and \$35-\$55 million in sales milestones. Cornerstone also is eligible for additional milestones if Targacept selects additional compounds. Cornerstone has rights to the patents and the library from the Feinstein Institute for Medical Research.

CyDex Pharmaceuticals Inc., Lenexa, Kan.
University of Kansas, Lawrence, Kan.
Business: Drug delivery

CyDex received exclusive, worldwide rights to the university's sulfoalkyl ether-alkyl ether cyclodextrin derivative for CyDex's Captisol sulfobutylether beta-cyclodextrin technology portfolio. The technology improves the solubility, stability, bioavailability, safety and dosing of active pharmaceutical ingredients (APIs). Cydex's Captisol-enabled melphalan is in Phase IIa testing as myeloablative conditioning in multiple myeloma (MM) patients undergoing autologous transplantation. The formulation uses CyDex's Captisol sulfobutylether beta-cyclodextrin technology. Further terms were not disclosed.

Cypress Bioscience Inc. (NASDAQ:CYPB), San Diego, Calif.
Business: Musculoskeletal, Neurology

Cypress' board rejected an unsolicited offer from shareholder Ramius LLC to acquire the 90.1% of the company it does not already own for \$4 per share. The offer values Cypress at about \$153.5 million based on 38.4 million shares outstanding at May 5 and is a 60% premium to the company's close of \$2.50 on July 16, before the offer was announced. The board said the offer undervalues Cypress and is not in the best interest of shareholders. Jefferies and Perella Weinberg Partners are advising Cypress (see *BioCentury*, July 26).

Evotec AG (Xetra:EVT), Hamburg, Germany
Boehringer Ingelheim GmbH, Ingelheim, Germany
Business: Inflammation, Autoimmune

Evotec received a €2.5 million (\$3.3 million) milestone payment from Boehringer under an amended 2004 deal to jointly identify and develop small molecules against GPCRs and other target classes. The payment was triggered by the selection of an undisclosed compound in the inflammation and immunology program for "pre-development" studies. This is the tenth milestone payment Evotec has received under the deal, which was amended last year to include oncology targets (see *BioCentury*, Nov. 26, 2009).

Five Prime Therapeutics Inc., San Francisco, Calif.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Business: Endocrine, Musculoskeletal

The companies will discover targets and drug candidates to treat skeletal muscle diseases, including sarcopenia and cachexia. Five Prime will conduct high-throughput *in vitro* and *in vivo* assays of its collection of secreted proteins and transmembrane receptor proteins. GSK will have the option to license exclusive rights for each target or candidate discovered. Five Prime will receive \$15 million, which includes an upfront payment, research payments for 2010 and an equity purchase by GSK. Five Prime is eligible for additional research payments during the remaining two years of the three-year deal and is eligible for up to \$124 million in option exercise fees and milestone payments for each product, plus royalties.

Forbes Medi-Tech Inc. (OTCBB:FMTI), Vancouver, B.C.
Marco Hi-Tech JV LLC, New York, N.Y.
Business: Metabolic

Forbes said supplement company Marco Hi-Tech increased its offer to acquire substantially all Forbes' assets to \$1.8 million in cash from \$1.4 million, plus inventory adjustments. The move comes after supplement company Pharmachem Laboratories Inc. (Kearny, N.J.) offered \$1.9 million in cash to acquire Forbes' assets last month. Forbes has the right to consider and accept a superior offer, and Marco Hi-Tech has the right to match any superior offer. The board of Forbes said it supports the Marco Hi-Tech offer and recommends shareholders approve the deal.

Following the sale, Forbes will wind down operations and anticipates distributing C\$0.14-C\$0.19 per share to its shareholders. Forbes' *See next page*

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assets include cholesterol-lowering food ingredient Reducol, to which Forbes reacquired rights from Novartis AG (NYSE:NVS; SIX:NOVN, Basel, Switzerland) in 2001 (see *BioCentury*, July 19 & July 26).

FTA Bioscience LLC, Cleveland, Ohio

Pure Bioscience (NASDAQ:PURE), El Cajon, Calif.

Business: Infectious

Pure Bioscience granted FTA exclusive, worldwide rights to develop and commercialize a topical silver dihydrogen citrate (SDC)-based product for onychomycosis and tinea pedis (athlete's foot). The electrolytically-generated source of stabilized ionic silver is in preclinical development. Pure Bioscience is eligible for milestones and royalties. Further terms were not disclosed.

Galapagos N.V. (Euronext:GLPG; Pink:GLPYY), Mechelen, Belgium

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.

Business: Autoimmune

Galapagos reacquired all rights to GLPG0634 for an undisclosed amount from GlaxoSmithKline, which had an option under an ongoing 2006 deal to license the arthritis candidate after Phase IIa testing. Galapagos plans to start a Phase I trial for the Janus kinase-1 (JAK-1) and JAK-2 inhibitor next week. GLPG0555, the lead compound under the deal, is a small molecule targeting an undisclosed kinase that has completed a Phase I trial. Galapagos plans to start another Phase I trial for the compound this half. Further terms were not disclosed (see *BioCentury*, July 12, 2006 & July 16, 2007).

GenSpera Inc. (OTCBB:GNSZ), San Antonio, Texas

Johns Hopkins University, Baltimore, Md.

University of Copenhagen, Copenhagen, Denmark

Business: Diagnostic

GenSpera acquired a patent application from the universities covering the creation of cancer-specific imaging compounds. The technology incorporates derivatives of thapsigargin coupled with tumor-targeted peptides to create imaging compounds that can detect and monitor tumors when used with imaging tools. The universities co-invented the technology. GenSpera is focused on the development of thapsigargin, a plant-derived cytotoxin, combined with a pro-drug delivery system that targets drug release only at the tumor site. GenSpera's lead compound G-202, a prodrug of plant-derived cytotoxin 12ADT, is in Phase I testing to treat solid tumors. Financial terms were not disclosed.

Lexicon Pharmaceuticals Inc. (NASDAQ:LXRX), The Woodlands, Texas

Symphony Icon Inc., Rockville, Md.

Business: Gastrointestinal

Lexicon exercised its option to acquire Symphony Icon. Lexicon gained the option in 2007 when it out-licensed gastrointestinal candidates to Symphony Icon, which was formed by private equity firm Symphony Capital and co-investors with a \$45 million investment. Symphony Icon will receive \$50 million in deferred payments, minus 50% of any development costs Lexicon incurs, with a maximum reduction of \$15 million. Additionally, Symphony Icon will receive 50% of any payments resulting from out-licensing any of the programs, up to \$30 million, unless the program has been approved in the U.S. If a program receives U.S. approval, Lexicon will make a payment to Symphony Icon of \$15 million in lieu of the out-licensing payments, plus whatever portion of deferred development costs are outstanding for that specific product. Under the deal, all payments made on or before July 30, 2012

will consist of at least 50% Lexicon stock. Payments made after that date will consist of no more than 50% stock (see *BioCentury*, June 25, 2007).

Lexicon regains tryptophan hydroxylase 1 (TPH1) inhibitors LX1031, which has completed a Phase II trial in diarrhea-predominant and mixed forms of irritable bowel syndrome (IBS-D and IBS-M); and LX1032, which is in Phase II testing to manage gastrointestinal symptoms associated with carcinoid syndrome. Lexicon also regains LX1033, a preclinical locally acting serotonin synthesis inhibitor. Lexicon said it is in discussions with potential partners to license the programs.

Middlebrook Pharmaceuticals Inc. (PINK:MBRKQ), Westlake, Texas

Victory Pharma Inc., San Diego, Calif.

Business: Infectious

Victory completed its previously announced acquisition of substantially all of Middlebrook's assets for \$17.3 million in cash (see *BioCentury*, May 24).

MorphoSys AG (Xetra:MOR), Martinsried, Germany

University College London, London, U.K.

Business: Antibodies

The university's UCL Business plc commercialization arm granted MorphoSys' AbD Serotec unit worldwide, exclusive rights to research and diagnostic applications of an antibody against parathyroid hormone (PTH). MorphoSys previously had a non-exclusive license to the antibody, under which it was supplying it to an undisclosed diagnostics company for use in PTH assays. MorphoSys said additional companies had expressed interest in supply agreements. Further terms were not disclosed.

Movetis N.V. (Euronext:MOVE), Turnhout, Belgium

Shire plc (LSE:SHP; NASDAQ:SHPGY), Basingstoke, U.K.

Business: Gastrointestinal, Hepatic

Shire proposed to acquire Movetis for €19 per share, or €428 million (\$559.5 million) in cash. The price is a 74% premium to Movetis' closing price of €10.90 on Aug. 2, the day before the deal was announced.

Shire said the deal would broaden its gastrointestinal portfolio and expand its presence in Europe, where Movetis markets Resolor prucalopride for chronic constipation in women in whom laxatives fail to provide adequate relief. Resolor is also in clinical testing for constipation in other populations. Movetis has rights to the serotonin (5-HT4) receptor agonist in Europe from Johnson & Johnson (NYSE:JNJ, Brunswick, N.J.), which spun out Movetis in 2006. Movetis is eligible for royalties on ex-European sales of Resolor from JNJ. Shire markets Lialda mesalamine for ulcerative colitis.

Shire would also gain M0002, a vasopressin 2 (V2) receptor antagonist in Phase II testing for liver ascites and M0003, a serotonin (5-HT4) receptor agonist in Phase II testing for gastroesophageal reflux disease (GERD).

Movetis' board unanimously supports the offer, and a group of institutional shareholders, including Sofinnova Partners, Sofinnova Ventures and Life Sciences Partners, who hold 38.9% of Movetis, have agreed to the deal. Shire plans to begin its tender offer in September and expects the deal to close this year. At March 31, Movetis had €100 million in cash. Deutsche Bank is advising Shire on the deal, and Evercore Partners is advising Movetis.

Osteologix Inc. (OTCBB:OLGX), Glen Allen, Va.

Servier, Neuilly-sur-Seine, France

Business: Musculoskeletal, Dental

Osteologix granted Servier exclusive, ex-U.S. rights to develop and commercialize NB S101 to treat postmenopausal osteoporosis, other

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bone and joint disorders, and dental indications. NBS101 is a strontium formulation which completed a Phase II trial to treat osteoporosis in 2007. Osteologix is eligible for up to €12 million (\$15.7 million) in upfront and milestone payments plus single-digit royalties on sales, plus additional milestones and royalties in Japan. Servier will be responsible for all ex-U.S. development costs (see *BioCentury*, Nov. 12, 2007).

Hard to Treat Diseases Inc. (Pink:HTDS), Clearwater, Fla.
Business: Neurology, Dermatology

Hard to Treat Diseases said it will sell its Slavica Biochem subsidiary to an undisclosed biomedical company. Slavica is a research center focused on the evaluation of therapies for neurological disorders, including multiple sclerosis (MS). Hard to Treat said the sale of Slavica along with its completed sale of its Collagenna Skin Care Products subsidiary will allow the company to focus on its China-based vaccine distributor Shenzhen Mellow Hope Pharm Industrial Co. Ltd. Axia Group Inc. (Pink:AGIJ, Cave Creek, Ariz.) acquired the natural health products and cosmetics company last month in a stock deal valued at \$10.5 million based on Axia's close of \$0.10 on July 29, the day before the deal closed. Financial terms for the Slavica sale were not disclosed.

Radiant Pharmaceuticals Corp. (NYSE-A:RPC), Tustin, Calif.
Shanxi BaoTai Pharmaceutical Co. Ltd., Taiyuan, China
Business: Pharmaceuticals

Radiant's Jade Pharmaceuticals Inc. subsidiary signed a letter of intent to acquire Chinese manufacturing company Shanxi in a stock deal. The companies plan to complete the transaction as a merger, after which Jade intends to merge with an undisclosed public company. The newly formed company will remain a subsidiary of Radiant. Jade expects to complete a bridge financing to fund expenses related to the merger with Shanxi and the subsequent merger with the public company. The merger between Jade and Shanxi is expected to close in mid-November. Financial terms were not disclosed.

Seattle Genetics Inc. (NASDAQ:SGEN), Bothell, Wash.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Business: Cancer

Seattle Genetics added antigens to a 2002 deal that gave Roche's Genentech Inc. unit rights to use Seattle Genetics' antibody-drug conjugate (ADC) technology. Seattle Genetics will receive \$12 million up front for the additional antigens, which will be chosen by Genentech. Genentech said it will focus on hematologic malignancies and solid tumors.

Seattle Genetics is now eligible for more than \$1.4 billion in milestones, including more than \$900 million under the expanded portion of the deal and over \$500 million under the original deal, plus mid-single digit royalties. Seattle Genetics has already received over \$30 million in milestones. Genentech is responsible for all preclinical and clinical development, as well as manufacturing and commercialization. In March, Seattle Genetics received an undisclosed milestone under the original deal after Genentech submitted an IND to FDA for an undisclosed ADC to treat cancer (see *BioCentury*, April 29, 2002 & March 8, 2010).

TapImmune Inc. (OTCBB:TPIV), Seattle, Wash.
Mayo Clinic, Rochester, Minn.
Business: Infectious

The clinic will conduct research combining peptide antigens with TapImmune's transporter associated with antigen processing (TAP) vaccine technology to develop a smallpox vaccine. TapImmune will have

an exclusive option to license worldwide rights to the vaccine after preclinical animal studies. Financial terms were not disclosed.

Vectura Group plc (LSE:VEC), Chippenham, U.K.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Business: Drug delivery

Vectura granted GlaxoSmithKline non-exclusive, worldwide rights to use its dry powder formulation technology for two products, 573719 and 642444. Vectura will receive £10 million (\$15.8 million) up front and is eligible for £10 million in milestones. Vectura also is eligible for up to £13 million (\$20.5 million) in annual royalties. 573719 is a muscarinic acetylcholine antagonist in Phase II testing to treat chronic obstructive pulmonary disease (COPD) as monotherapy and in combination with 642444. GSK has rights from Theravance Inc. (NADAQ:THRX, South San Francisco, Calif.) to 642444, which is a long-acting adrenergic receptor beta 2 agonist (LABA) in Phase III testing for COPD.

SALES & MARKETING

Celera Corp. (NASDAQ:CRA), Alameda, Calif.
Business: Pharmacogenetics

Celera disclosed in its 2Q10 earnings that in July its Berkeley HeartLab Inc. subsidiary launched a test in the U.S. to identify carriers of genetic variants of the Cytochrome P450 2C19 (CYP2C19) gene. Genetic variants of the gene may affect the efficacy of cardiovascular drug Plavix clopidogrel. Bristol-Myers Squibb Co. (NYSE:BMJ, New York, N.Y.) and sanofi-aventis Group (Euronext:SAN; NYSE:SNY, Paris, France) market Plavix. The cost of the test was not disclosed.

OTHER NEWS

Alcon Inc. (NYSE:ACL), Hünenberg, Switzerland
Nestle S.A. (SIX:NESN), Vevey, Switzerland
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Business: Ophthalmic

Alcon's independent committee of directors said that proxy advisory services RiskMetrics Group Inc. and Glass Lewis & Co. recommended that Alcon's minority shareholders vote against all five of Novartis' designees to Alcon's board of directors at an Aug. 16 shareholders meeting. In January, the pharma excised an option to acquire Nestle's 52% stake in the company at \$180 per share. Novartis also made a subsequent offer to acquire the remaining 23% not owned by Nestle in a stock deal valued at \$151.43 per share, an offer the committee rejected. Last month the committee formed the Alcon Litigation trust to provide financial support to protect the interest of Alcon and its minority shareholders (see *BioCentury*, July 19).

Cleveland BioLabs Inc. (NASDAQ:CBLI), Buffalo, N.Y.
U.S. Department of Health and Human Services, Washington, D.C.

Business: Other

Cleveland BioLabs will receive a \$4.1 million payment from HHS's Biomedical Advanced Research and Development Authority (BARDA) after BARDA exercised a fourth option under a September 2008 contract for up to \$15.6 million to develop the biotech's Protectan (CBLB502) to treat acute radiation syndrome (ARS). The option supports validation of the CBLB502 manufacturing process, manufacturing of three additional registration batches of the drug and additional animal studies. The radioprotectant derivative of flagellin, which is being developed under FDA's animal efficacy rule, is in Phase IIa testing, with a Phase IIb trial slated for this year. Cleveland BioLabs has already

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received \$8.2 million in three previous milestones payments. In September 2009, BARDA exercised its first option to increase the amount of the three-year contract to \$15.6 million from \$13.3 million and provided \$6.3 million to the biotech. Protectant has Fast Track designation from FDA to reduce the risk of death following total body irradiation during or after a radiation disaster.

Cypress Bioscience Inc. (NASDAQ:CYPB), San Diego, Calif.

Forest Laboratories Inc. (NYSE:FRX), New York, N.Y.

Business: Musculoskeletal, Neurology

Cypress will restructure and reduce headcount by 123 (86%) to 20 after it discontinued co-promotion of fibromyalgia drug Savella milnacipran in the U.S. with partner Forest. The cuts come from the company's commercial business. Cypress, which remains eligible for royalties on Savella, said it "may pursue the opportunity to re-activate the co-promotion right." Cypress will receive a one-time payment from Forest of \$2 million. Forest reported \$53 million in U.S. sales of Savella in the fiscal year ending March 31.

Cypress licensed U.S. and Canadian rights to the norepinephrine and serotonin reuptake inhibitor (NSRI) from Laboratoires Pierre Fabre S.A. (Castres, France) in 2001. Cypress then partnered with Forest to develop and commercialize Savella in 2004 (see *BioCentury*, Jan. 19, 2009 & April 27, 2009).

Cypress also plans to discontinue or sell its personalized medicine services business by the end of 3Q10. The unit markets diagnostics for rheumatoid arthritis and to measure methotrexate treatment for RA. At March 31, Cypress reported three-month revenue of \$195,713 for the business, which it acquired through its 2008 acquisition of Proprius Pharmaceuticals Inc.

Cypress plans to focus on CYP-1020 (formerly BL-1020), a GABA enhanced antipsychotic agent that has completed a Phase IIb trial to treat schizophrenia. Cypress received North American rights to the product from BioLineRx Ltd. (Tel Aviv:BLRX, Jerusalem, Israel) earlier this year. An additional Phase IIb trial to treat cognitive deficits associated with schizophrenia is planned for 1Q11 (see *BioCentury*, June 28).

Cypress expects the commercial cuts to save \$10 million annually. At March 31, Cypress had \$137.3 million in cash and a three-month operating loss of \$4.8 million. The company had a 2009 operating loss of \$29.9 million.

Elusys Therapeutics Inc., Pine Brook, N.J.

U.S. Department of Health and Human Services, Washington, D.C.

Business: Infectious

HHS's Biomedical Advanced Research and Development Authority (BARDA) awarded Elusys a second contract year of funding valued at \$40.6 million to develop Anthim to prevent and treat anthrax infection. Elusys has already received \$16.8 million under the five-year contract, which is valued at up to \$143 million. Anthim is an affinity enhanced mAb against the *Bacillus anthracis* protective antigen and has Orphan Drug and Fast Track designations in the U.S. It is being developed under FDA's Animal Rule, under which marketing approval can be granted based on efficacy in relevant animal models and an acceptable safety risk profile in humans, and has completed two human safety studies (see *BioCentury*, Jan. 4).

Genzyme Corp. (NASDAQ:GENZ), Cambridge, Mass.

U.S. Department of Health and Human Services, Washington, D.C.

Business: Metabolic

Three Fabry's disease patients petitioned HHS to exercise march-in powers under the federal Bayh-Dole Act for an open license to patents covering Genzyme's Fabrazyme agalsidase beta. The Bayh-Dole Act allows the government to make federally-funded inventions available to the public under certain circumstances, including when "action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees." The petitioners argue that as Fabrazyme was discovered using grant funding from the National Institutes of Health and that Genzyme's manufacturing issues have caused a shortage leading to rationing of the drug, that HHS has the authority to grant an open license under Bayh-Dole. The petitioners call for a 5% royalty to Genzyme on the sales of any agalsidase beta products made under the open license.

Fabrazyme supply has been limited since a vesivirus infection temporarily shut down the plant where it is made last year. Genzyme, which is currently shipping Fabrazyme at levels to meet 30% of demand, said that it is on track to increase shipments in 4Q10. Genzyme added that the approval of biologics manufacturing facilities can take years.

Lpath Inc. (OTCBB:LPTN), San Diego, Calif.

Business: Ophthalmic

Lpath received a \$3 million grant from the BRDG-SPAN program at NIH's National Eye Institute to support Phase II development of Lpath's iSONEP sphingomab for wet age-related macular degeneration (AMD). The ocular formulation of humanized Sphingomab, a mAb against the sphingosine 1-phosphate (S1P) receptor, is in Phase I testing for the indication. In March, Merck KGaA (Xetra:MRK, Darmstadt, Germany) terminated a 2008 deal with Lpath to develop Asonop sphingomab after Lpath rejected Merck's proposal to extend the deadline by which the company had to opt-in to further development. Lpath said it plans to seek a new partner for the program (see *BioCentury*, April 5).

The Medicines Co. (NASDAQ:MDCO), Parsippany, N.J.

Business: Cardiovascular

The U.S. Patent and Trademark Office (PTO) granted a one-year interim extension for a patent covering anticoagulant Angiomax bivalirudin from The Medicines Co. The decision follows a ruling earlier in the week by the U.S. District Court for the Eastern District of Virginia ordering the PTO to consider the company's application for an extension as timely filed.

The PTO denied the application in March, claiming the company had missed the 60-day filing window by two days. In his decision, Judge Claude Hilton said PTO interpreted the Hatch-Waxman Act in a manner that deprives an applicant of the full 60 days to submit an extension application (see *BioCentury*, March 29).

Under the one-year extension, the PTO will determine how long to extend the patent. Medicines Co. is seeking an extension to December 2014. The patent had been set to expire on May 23 but the court ordered the PTO to ensure that the patent does not expire until at least 10 days after the court issues a decision in the case (see *BioCentury*, May 24).

Additionally, the judge ordered the PTO to consider NDA approvals received by a company after close of business to have been received on the next business day, rather than the same day, for the purpose of determining patent extension filing deadlines. In the case, Medicines Co. claimed both FDA and PTO had misinterpreted the filing deadlines regarding the application. FDA could not be reached for comment. The small molecule direct thrombin inhibitor had U.S. sales of \$200.8 million in 1H10.

NicOx S.A. (Euronext:COX), Sophia-Antipolis, France

Business: Autoimmune

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NicOx will close its U.S. headquarters, NicOx Inc., effective Aug. 31 after FDA issued a complete response letter for an NDA for naproxcinod to treat signs and symptoms of osteoarthritis (OA). The closure of the facility, which is responsible for commercial and clinical activities, will result in headcount reductions of 22 (18%) to 102. Naproxcinod is a cyclooxygenase (COX)-inhibiting nitric oxide donator (CINOD) that releases naproxen and nitric oxide.

The closure is expected to reduce cash burn by an undisclosed amount. At June 30, NicOx had €128.4 million (\$156.9 million) in cash and six-month operating loss of €27.4 million (\$33.4 million) (see *BioCentury*, July 26).

Pfenex Inc., San Diego, Calif.

U.S. Department of Health and Human Services, Washington, D.C.

Business: Infectious

Pfenex received a contract for up to \$18.8 million in funding from the HHS' Biomedical Advanced Research and Development Authority (BARDA) to develop a process for the production of bulk recombinant protective antigen (rPA) from anthrax. Pfenex will use its Pfenex Expression Technology to identify strains of anthrax that are capable of producing high titers of stable rPA and will then develop a cGMP process at commercial production scales. Pfenex will subsequently conduct preclinical testing of the protein. Pfenex Expression Technology is a *Pseudomonas fluorescens*-based recombinant protein expression technology.

Servier, Neuilly-sur-Seine, France

Business: Cardiovascular, Endocrine, Neurology

The European Commission (EC) sent Servier a statement of objections under EU antitrust rules for providing misleading and incorrect information in a reply to a request for information related to pharmaceutical competition. The EC said the next step is for Servier to reply in writing or request an oral hearing to present their comments on the case to EC representatives and the national competition authorities. Servier could be fined up to 1% of its total sales in the preceding business year if it concludes Servier intentionally or negligently provided misleading and incorrect information. Servier said the statement does not prejudice the final outcome of the investigation and that the company is fully cooperating with the EC on the matter. Further details were not disclosed.

Vectura Group plc (LSE:VEC), Chippenham, U.K.

Business: Drug delivery, Pulmonary, Neurology

Vectura will restructure its R&D operations and reduce headcount by about 85 (31%) to 190 to focus on partnered programs and branded generics. Vectura will seek licensing partners for its existing specialty products, including VR040, an inhaled apomorphine in Phase II testing to treat Parkinson's disease (PD); and VR496, an inhaled mucolytic agent in Phase II testing to treat cystic fibrosis (CF).

The cuts, which include the proposed closure of a Nottingham, U.K., R&D facility, are expected to save about £6 million (\$9.5 million) annually beginning in the fiscal year starting April 1, 2011. At March 31, Vectura had £64.1 million in cash (\$96.8 million) and a 12-month operating loss £15.3 million (\$23.1 million).

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MANAGEMENT TRACKS

Boards of Directors

Penwest Pharmaceuticals Co. (NASDAQ:PPCO), Patterson, N.Y.

Business: Drug delivery

Appointed: Kevin Tang as chairman, currently managing director of Tang Capital Management LLC

Management

Aragon Pharmaceuticals Inc., San Diego, Calif.

Business: Cancer

Promoted: Co-founder Richard Heyman to CEO while remaining president and head of R&D

AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.

Business: Pharmaceuticals

Hired: Scott Carmer as EVP of commercial operations of AstraZeneca's MedImmune LLC unit, formerly VP of sales and marketing for the rheumatology franchise of Roche's Genentech Inc. unit

BioAlliance Pharma S.A. (Euronext:BIO), Paris, France

Business: Cancer, Infectious, Drug delivery

Promoted: Pierre Attali to COO, while remaining CMO

Resigned: Gilles Avenard as deputy CEO and a director

CT Atlantic AG, Zurich, Switzerland

Business: Cancer, Antibodies

Hired: Michael Hoecker as CEO, formerly global medical director at Roche

Promoted: Cara Lerner to COO from head of program management

Formac Pharmaceuticals N.V., Leuven, Belgium

Business: Drug delivery

Hired: Filip Kiekens as CSO, formerly principal scientist at the Janssen Pharmaceutica N.V. unit of Johnson & Johnson; and Laurent Schueller as COO, formerly chemical and pharmaceutical team leader at J&J's Tibotec Pharmaceuticals Ltd. unit

Living Cell Technologies Ltd. (ASX:LCT; OTCQX:LVCLY), Sydney, Australia

Business: Gene/Cell therapy, Endocrine, Neurology

Hired: Ross Macdonald as managing director, formerly VP of business development at Sinclair Pharmaceuticals Ltd.

Lupin Ltd. (NSE:LUPIN; BSE:500257), Mumbai, India

Business: Pharmaceuticals

Hired: Paul McGarty as president of Lupin's U.S. subsidiary, Lupin Pharmaceuticals Inc., formerly CEO of Nycomed's Nycomed U.S. Inc. subsidiary

Nycomed, Zurich, Switzerland

Business: Pharmaceuticals

Hired: Jeffrey Wasserstein as SVP of business development and strategy at Nycomed's Nycomed U.S. Inc. subsidiary, formerly president of Dr. Reddy's Laboratories Ltd.'s Promius Pharma LLC subsidiary

PharmaGap Inc. (TSX-V:GAP), Ottawa, Ontario

Business: Cancer, ADMET

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CLINICAL NEWS

Clinical activities and selected announcements for the week ended August 6.

REGULATORY

Abbott Laboratories (NYSE:ABT), Abbott Park, Ill.

Product: Meridia sibutramine

Business: Endocrine

FDA's Endocrinologic and Metabolic Drugs Advisory Committee will meet on Sept. 15 to discuss cardiovascular safety signals seen in the long-term Phase III SCOUT trial of anti-obesity drug Meridia sibutramine from Abbott. Abbott markets the serotonin, norepinephrine and dopamine reuptake inhibitor as Meridia in the U.S. The drug was approved in Europe as Reductil, Reduxade and Zelium. In January, FDA concluded a safety review of Meridia and requested the label include a new contraindication stating that the drug is not to be used in patients with a history of cardiovascular disease (see *BioCentury*, Jan. 25). In the same month, the CHMP, part of the European Medicines Agency (EMA), recommended a marketing suspension of sibutramine.

Abraxis BioScience Inc. (NASDAQ:ABII), Los Angeles, Calif.

Otsuka Pharmaceutical Co. Ltd. (Tokyo:4768), Tokyo, Japan

Product: Abraxane nab-paclitaxel

Business: Cancer

Abraxis said that Abraxane nab-paclitaxel was granted marketing approval in New Zealand to treat metastatic breast cancer after failure of anthracycline therapy. Specialised Therapeutics Australia Pty. Ltd. (East Kew, Australia), which already markets Abraxane in Australia, will launch the albumin stabilized nanoparticle formulation of paclitaxel in New Zealand after receiving reimbursement approval. Abraxane is approved in 41 countries including the U.S. and EU, as well as Japan, where Otsuka has rights to the product. Abraxis is being acquired by Celgene Corp. (NASDAQ:CELG, Summit, N.J.) (see *BioCentury*, July 5).

Acceleron Pharma Inc., Cambridge, Mass.

Product: ACE-031

Business: Musculoskeletal

FDA granted Fast Track designation for Acceleron's ACE-031 to treat Duchenne muscular dystrophy (DMD). The myostatin (GDF-8) inhibitor is currently in Phase II testing for the indication.

Acrux Ltd. (ASX:ACR), Melbourne, Australia

Vivus Inc. (NASDAQ:VVUS), Mountain View, Calif.

Product: EvaMist estradiol MDTs (Ellavie)

Business: Endocrine

FDA issued a warning about inadvertent exposure of EvaMist to children and animals through skin contact that could result in adverse effects. Since the drug was approved in July 2007 through June 2010, FDA said it has received 8 reports of inadvertent exposure in children ages 3-5 that have resulted in premature puberty, nipple swelling and breast development in females, as well as breast enlargement in males. The agency also noted 2 cases of secondary exposure in dogs that have resulted in nipple enlargement and vulvar swelling. FDA plans to continue reviewing related reports.

Acrux licensed EvaMist to Vivus, which subsequently granted U.S. marketing rights to KV Pharmaceutical Co. (NYSE:KVA, St. Louis, Mo.). KV markets the estradiol delivered via metered-dose transdermal spray to treat moderate to severe vasomotor symptoms due to menopause.

AdvanDx Inc., Woburn, Mass.

Product: Yeast Traffic Light PNA FISH

Business: Diagnostic

FDA granted 510(k) clearance for a 90-minute protocol for AdvanDx's Yeast Traffic Light PNA FISH to identify *Candida* species from blood cultures. bioMerieux S.A. (Euronext:BIM, Marcy l'Etoile, France) has U.S. marketing rights to the PNA FISH testing platform under a 2007 deal. In 2008, FDA approved a 2.5-hour version of the nucleic acid hybridization assay (see *BioCentury*, Sept. 29, 2008).

Affymax Inc. (NASDAQ:AFFY), Palo Alto, Calif.

Takeda Pharmaceutical Co. Ltd. (Tokyo:4502), Osaka, Japan

Product: Hematide peginesatide

Business: Hematology

Affymax and partner Takeda said they plan to submit an NDA for Hematide peginesatide to treat anemia in chronic kidney disease (CKD) in dialysis patients in H111. The timeline will be finalized following a meeting with FDA that is expected to be held by year end. The companies will continue to evaluate the synthetic peptide-based eryth-

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Management Tracks, from previous page

Hired: Ken Sokoll as COO and VP of clinical development, effective Sept. 1, formerly VP of drug development at Milestone Pharmaceuticals Inc.

Pharminox Ltd., Oxford, U.K.

Business: Cancer

Hired: Marc Hummersone as research director

Transitioning: Malcolm Stevens from CSO and a director to CSO emeritus

Photocure ASA (OSE:PHO), Oslo, Norway

Business: Cancer, Dermatology

Hired: Terry Conrad as president of Photocure's newly established U.S. subsidiary, Photocure Inc., formerly president and CEO of Merz GmbH & Co. KGaA's Merz Pharmaceuticals LLC

Signum Biosciences Inc., Monmouth Junction, N.J.

Business: Dermatology, Neurology, Endocrine

Hired: Braham Shroot as CEO, formerly CSO of Barrier Therapeutics Inc., which is now part of GlaxoSmithKline plc; he replaces Gregory Stock, who will remain a director

Tengion Inc. (NASDAQ:TNGN), East Norriton, Pa.

Business: Genitourinary, Gene/Cell therapy, Transplant

Hired: A. Brian Davis as CFO, formerly SVP and CFO of Neose Technologies Inc.

Tolerx Inc., Cambridge, Mass.

Business: Endocrine, Autoimmune

Hired: Antonin de Fougères as CSO, formerly VP of research, immunology, metabolic and viral disease at Alnylam Pharmaceuticals Inc.

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ropoiesis-stimulating agent (ESA) in non-dialysis patients.

In June, the partners reported that Hematide led to an increased incidence of cardiovascular events compared to Aranesp darbepoetin alfa in the Phase III PEARL 1 and 2 trials in non-dialysis patients. The safety signal was not observed in the Phase III EMERALD 1 and 2 trials in dialysis patients. All 4 trials met their respective primary endpoints (see *BioCentury*, June 28). Amgen Inc. (NASDAQ:AMGN, Thousand Oaks, Calif.) markets Aranesp.

Allergan Inc. (NYSE:AGN), Irvine, Calif.

Product: Ozurdex dexamethasone intravitreal implant (formerly Posurdex)

Business: Ophthalmic

Allergan said the European Commission approved an MAA for Ozurdex dexamethasone intravitreal implant to treat macular edema following retinal vein occlusion. Allergan, which plans to launch the biodegradable implant in Europe this quarter, obtained the product in its 2003 acquisition of Oculex Pharmaceuticals Inc. (see *BioCentury*, June 22, 2009).

Allergan Inc. (NYSE:AGN), Irvine, Calif.

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.

Product: Botox onabotulinumtoxinA (BTX-A) (formerly botulinum toxin)

Business: Neurology

Allergan said that FDA extended by three months the PDUFA date for an sBLA for Botox onabotulinumtoxinA to treat chronic migraine. Allergan had submitted a modified REMS for the vacuum-dried purified botulinum toxin type A at FDA's request. Botox is approved in the U.S. to treat severe primary axillary hyperhidrosis, cervical dystonia and strabismus, blepharospasm associated with dystonia and upper limb spasticity. The PDUFA date is not disclosed. GlaxoSmithKline has rights to the product in China and Japan from Allergan (see *BioCentury*, Oct. 10, 2005).

Arena Pharmaceuticals Inc. (NASDAQ:ARNA), San Diego, Calif.

Product: Lorcaserin (APD356)

Business: Endocrine

Arena said FDA confirmed a meeting of the Endocrinologic and Metabolic Drugs Advisory Committee on Sept. 16 to discuss an NDA for lorcaserin for weight management. In June, Arena said FDA had tentatively scheduled the meeting for the date. The serotonin (5-HT_{2C}) receptor agonist has an Oct. 22 PDUFA date. Eisai Co. Ltd. (Tokyo:4523; Osaka:4523, Tokyo, Japan) has exclusive marketing rights to lorcaserin in the U.S. (see *BioCentury*, July 5).

Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan

Product: Mirabegron (YM178)

Business: Genitourinary

Astellas disclosed in its quarterly financial results that it submitted an NDA in Japan for mirabegron to treat urinary frequency, urinary incontinence or urgency associated with overactive bladder. The adrenergic receptor beta 3 (ADRB3) agonist is in Phase III testing for the indication in the EU and the U.S., with an NDA submission planned for this year.

Bayer AG (Xetra:BAY), Leverkusen, Germany

Product: Nimotop nimodipine

Business: Neurology

FDA issued a warning to remind healthcare professionals that oral nimodipine capsules should not be administered intravenously due to the risk of death, cardiac arrest, decreases in blood pressure and other heart-related complications. The agency said it continues to receive reports of adverse events resulting from IV administration of nimodipine despite having added a black box warning to the drug's label in 2006. Bayer markets the calcium channel blocker as Nimotop to improve neurological outcomes after subarachnoid hemorrhage.

Boehringer Ingelheim GmbH, Ingelheim, Germany

Bristol-Myers Squibb Co. (NYSE:BMJ), New York, N.Y.

sanofi-aventis Group (Euronext:SAN; NYSE:SNY), Paris, France

Product: Asasantin Retard dipyridamole (Aggrenox); Persantin Retard dipyridamole; Plavix clopidogrel

Business: Cardiovascular

The U.K.'s NICE issued a preliminary appraisal recommending wider use of clopidogrel due to the availability of cheaper generic versions of the antiplatelet drug in the U.K. The agency now recommends use of the adenosine diphosphate (ADP) receptor antagonist to prevent occlusive vascular events in patients who have had an ischemic stroke or have peripheral arterial disease or multivascular disease, or patients who have had a myocardial infarction (MI) if aspirin is contraindicated or not tolerated. The appraisal also recommends the use of Aggrenox/Asasantin Retard, a modified-release dipyridamole with aspirin, to prevent occlusive vascular events in patients who have had a transient ischemic attack or an ischemic stroke only if clopidogrel is contraindicated or not tolerated. Persantin Retard, modified-release dipyridamole alone, is recommended to prevent occlusive vascular events in patients who have had an ischemic stroke only if aspirin and clopidogrel are contraindicated or not tolerated, and in patients who have had a transient ischemic attack if aspirin is contraindicated or not tolerated. Comments on the appraisal are due Aug. 25, with a second appraisal meeting scheduled for Sept. 8.

The appraisal is a review of 2005 guidance, which previously recommended the first-line treatment in patients who have suffered a stroke or transient ischemic attack (TIA) for a period of 2 years from the most recent event. Bristol-Myers and sanofi-aventis market Plavix clopidogrel. Boehringer Ingelheim markets Asasantin Retard and Persantin Retard.

Celldex Therapeutics Inc. (NASDAQ:CLDX), Needham, Mass.

Product: CDX-011 (formerly CR011-vcMMAE)

Business: Cancer

FDA granted Fast Track designation for Celldex's CDX-011 to treat advanced, refractory/resistant glycoprotein NMB (GPNMB)-expressing breast cancer. This quarter, the company plans to start a Phase IIb trial of the human mAb against GPNMB linked to tubulin inhibitor monomethyl auristatin E (MMAE) for heavily pre-treated breast cancer.

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BioCentury Part II

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CSL Ltd. (ASX:CSL), Melbourne, Australia
Product: Afluria
Business: Infectious

FDA updated the label for CSL's Afluria to warn that the trivalent inactivated seasonal influenza vaccine has been associated with an increased incidence of fever and febrile seizure in Australian children, mainly under the age of 5 years. FDA said available data suggests that the increased incidence is only associated with the Southern Hemisphere formulation of the vaccine. FDA said it is requiring CSL to conduct a study of Afluria in children to obtain additional information regarding the febrile events. CSL will not supply 0.25 ml single-dose, prefilled syringes in the U.S., which are used in very young children. Afluria is approved for active immunization of persons aged 6 months and older against influenza virus subtypes A and B. Merck & Co. Inc. (NYSE:MRK, Whitehouse Station, N.J.) markets Afluria in the U.S (see *BioCentury*, Oct. 5, 2009).

Dendreon Corp. (NASDAQ:DNDN), Seattle, Wash.
Product: Provenge sipuleucel-T
Business: Cancer

Dendreon said that it asked the Centers for Medicare & Medicaid Services (CMS) to reconsider whether a National Coverage Analysis is necessary for the use of Provenge sipuleucel-T to treat metastatic, castrate-resistant prostate cancer. Dendreon said there is "overwhelming clinical evidence showing a significant improvement in overall survival in this patient population." FDA approved the autologous cellular immunotherapy in April. CMS expects to complete its analysis by June 30, 2011.

Dendreon also said that 9 local Medicare Administrative Contractors (MACs) have published coverage guidelines, and an additional 5 MACs have provided confirmation that the autologous cellular immunotherapy would be covered. One MAC representing Arkansas, Louisiana and Mississippi has issued confirmation of non-coverage for Provenge. Dendreon also has secured national and local coverage with major private plans (see *BioCentury*, July 5).

Devax Inc., Lake Forest, Calif.
Product: Axxess drug eluting stent
Business: Cardiovascular

Devax received CE Mark approval in the EU for its Axxess biolimus A9-eluting stent to treat coronary bifurcations. Devax has rights to biolimus A9 from BioSensors International Group Ltd. (Singapore).

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Product: Veltin Gel clindamycin/tretinoin
Business: Dermatology

FDA approved Veltin clindamycin/tretinoin gel from GSK's Stiefel Laboratories Inc. subsidiary to treat acne vulgaris in patients 12 years and older. The company plans to launch the topical gel containing 1% clindamycin and 0.025% tretinoin later this year.

Isotechnika Pharma Inc. (TSX:ISA), Edmonton, Alberta
Lux Biosciences Inc., Jersey City, N.J.
Product: Luveniq voclosporin (LX211)
Business: Ophthalmic

Lux received a complete response letter from FDA for an NDA for Luveniq voclosporin to treat non-infectious uveitis in the intermediate or posterior segments of the eye. According to Lux, FDA said in the letter that it considers data from only 1 of the 2 pivotal trials included in the application as supportive for approval. The company plans to

begin an additional pivotal trial of Luveniq this year.

Last year, Lux reported that Luveniq missed the primary endpoint of all-cause therapeutic failure vs. placebo in the Phase III LX211-02 trial, but met the primary endpoint of mean change from baseline in vitreous haze vs. placebo in the Phase III LX211-01 trial (see *BioCentury*, March 30, 2009). An MAA for the transisomer of a cyclosporine analog that inhibits calcineurin is under review in Europe, with a decision expected in Q111. Lux has rights to Luveniq for ophthalmic indications from Isotechnika.

Jazz Pharmaceuticals Inc. (NASDAQ:JAZZ), Palo Alto, Calif.
Product: Sodium oxybate (JZP-6)
Business: Musculoskeletal

UCB Group (Euronext:UCB, Brussels, Belgium) disclosed in its 2Q10 financial results that it submitted an MAA to European Medicines Agency (EMA) for Xyrem sodium oxybate to treat fibromyalgia. The company expects a decision in H111. UCB has ex-North American commercialization rights to the oral liquid formulation of the sodium salt of gamma hydroxybutyrate (GHB) for fibromyalgia from Jazz, which markets it in the U.S. as Xyrem to treat excessive daytime sleepiness and cataplexy in patients with narcolepsy.

Merz GmbH & Co. KGaA, Frankfurt, Germany
Product: Xeomin (NT 201)
Business: Neurology

FDA approved a BLA from Merz for Xeomin incobotulinumtoxinA to treat cervical dystonia and blepharospasm. The label includes a boxed warning about the risk of botulinum toxin spreading from the area of injection, which can cause swallowing and breathing difficulties. Merz expects to launch the botulinum neurotoxin type A by the end of September.

Movetis N.V. (Euronext:MOVE), Turnhout, Belgium
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Product: Resolor prucalopride
Business: Gastrointestinal

The U.K.'s NICE issued a preliminary appraisal recommending Resolor prucalopride to treat constipation in women who have tried at least two different types of laxative and lifestyle changes for at least 6 months, but have not had relief from constipation. NICE is accepting comments on the draft guidance until Aug. 24. Movetis has rights to the serotonin (5-HT4) receptor agonist in Europe from Johnson & Johnson, which spun out Movetis in 2006.

Separately, Movetis received marketing approval in Switzerland for Resolor to treat idiopathic chronic constipation in adults not responding to dietary measures and laxatives. SwissMedic added labelling to the drug to indicate that there was not sufficient data to demonstrate its safety and effectiveness in men, though it did not restrict the indication to use only in women. Shire plc (LSE:SHP; NASDAQ:SHPGY, Basingstoke, U.K.) proposed to acquire Movetis last week.

Progenics Pharmaceuticals Inc. (NASDAQ:PGNX), Tarrytown, N.Y.

Ono Pharmaceutical Co. Ltd. (Tokyo:4528; Osaka:4528), Osaka, Japan
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Product: Relistor methylalntrexone (MNTX) (MOA-728, ONO-3849)
Business: Gastrointestinal

The CHMP issued a positive opinion to grant marketing approval for a pre-filled syringe delivery system for subcutaneous Relistor methylalntrexone to treat opioid-induced constipation in patients receiving palliative care. The peripheral mu opioid receptor antagonist

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is marketed in single-use vials in the U.S., EU, Australia, Canada and several Latin American countries. An sNDA for the pre-filled syringe delivery system for Relistor is also under review at FDA. Progenics expects to launch the pre-filled syringes in the U.S. and EU in 2Q11. Wyeth, which Pfizer acquired last year, and Progenics co-developed Relistor. Ono has rights to the subcutaneous formulation of the product in Japan. The CHMP is part of the European Medicines Agency (EMA).

sanofi-aventis Group (Euronext:SAN; NYSE:SNY), Paris, France
Product: Taxotere docetaxel
Business: Cancer

FDA approved a one-vial formulation of cancer drug Taxotere docetaxel. The new formulation eliminates the need for health care professionals to perform an initial dilution step that was required when using the two-vial formulation, which consisted of docetaxel concentrate and a diluent. The microtubule-stabilizing taxoid is approved to treat metastatic and adjuvant breast cancer, metastatic androgen-independent prostate cancer, advanced non-small cell lung cancer (NSCLC), advanced gastric adenocarcinoma and locally advanced squamous cell carcinoma of the head and neck (SCCHN). sanofi-aventis expects to launch the one-vial formulation in 80 and 20 mg dosages this fall.

Product: Taxotere docetaxel
Business: Cancer

The European Medicines Agency (EMA) approved an MAA to extend the indication for Taxotere docetaxel from sanofi-aventis to include adjuvant treatment of early-stage, node-negative breast cancer in combination with doxorubicin and cyclophosphamide. The microtubule-stabilizing taxoid is approved to treat metastatic and adjuvant breast cancer, metastatic androgen-independent prostate cancer, advanced non-small cell lung cancer (NSCLC), advanced gastric adenocarcinoma and locally advanced squamous cell carcinoma of the head and neck (SCCHN).

Shire plc (LSE:SHP; NASDAQ:SHPGY), Basingstoke, U.K.
Dainippon Sumitomo Pharma Co. Ltd. (Tokyo:4506; Osaka:4506), Osaka, Japan
Product: Replagal agalsidase alfa
Business: Metabolic

Shire disclosed in its 2Q10 financial results that it withdrew a rolling BLA for Replagal agalsidase alfa to treat Fabry's disease. On a conference call, Shire said the prolonged shortage of Fabrazyme agalsidase beta from Genzyme Corp. (NASDAQ:GENZ, Cambridge, Mass.) will allow Shire to gather additional data to enhance the clinical portion of the application and potentially obtain a better label. Shire is already providing access to the injectable alpha-galactosidase A (Alpha-gal A) enzyme in the U.S. under a treatment protocol. Fabrazyme has faced supply shortages since June 2009 due to viral contamination and other problems at Genzyme's Allston, Mass. facility (see *BioCentury*, Oct. 26, 2009).

Replagal is already marketed for the indication in 45 countries, including in the EU, and has Fast Track designation in the U.S. Dainippon has Japanese rights for Replagal from Shire.

Xoma Ltd. (NASDAQ:XOMA), Berkeley, Calif.
Product: XOMA 052 (formerly XMA005.2)
Business: Inflammation

The COMP issued a positive opinion to grant Orphan Drug designation to Xoma's XOMA 052 to treat Behcet's disease. The humanized IgG2 mAb against IL-1 beta is in Phase II testing for the indication. COMP is part of the European Medicines Agency (EMA).

Product: XOMA 052 (formerly XMA005.2)
Business: Inflammation

FDA granted Orphan Drug designation for Xoma's XOMA 052 to treat Behcet's disease. The humanized IgG2 mAb against interleukin-1 (IL-1) beta is in Phase II testing for the indication.

CLINICAL RESULTS

Bayer AG (Xetra:BAY), Leverkusen, Germany
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Product: Xarelto rivaroxaban (BAY 59-7939)
Business: Cardiovascular

Molecular target: Factor Xa
Description: Direct Factor Xa inhibitor
Indication: Treat acute symptomatic deep vein thrombosis (DVT) without symptoms of pulmonary embolism (PE)
Endpoint: Cumulative incidence of symptomatic recurrent venous thromboembolism (VTE), non-fatal PE and fatal PE; composite of major and clinically relevant non-major bleeding
Status: Phase III data
Milestone: Additional Phase III data (08/31/2010)

The open-label, international Phase III EINSTEIN-DVT trial in >3,400 patients showed that oral rivaroxaban was non-inferior to current standard therapy (initial Lovenox enoxaparin followed by a vitamin K antagonist) on the primary endpoint of the cumulative incidence of symptomatic recurrent VTE. Additionally, rivaroxaban significantly improved net clinical benefit, a pre-specified secondary endpoint defined as the composite of the primary endpoint plus major bleeding, vs. standard therapy. Rivaroxaban was well tolerated, and the composite rate of major and clinically relevant non-major bleeding was similar between treatment groups. Patients received 15 mg twice-daily oral rivaroxaban for 3 weeks, followed by 20 mg once-daily rivaroxaban for 3, 6 or 12 months, or standard therapy. Data will be presented at the European Society of Cardiology meeting in Stockholm later this month.

J&J said it plans to respond by year end to a June 2009 complete response letter from FDA for an NDA for rivaroxaban to prevent DVT and PE in patients undergoing hip or knee replacement surgery (see *BioCentury*, June 1, 2009 & March 8, 2010). J&J has U.S. rights to rivaroxaban from Bayer, which markets it as Xarelto in more than 75 countries, including the EU. sanofi-aventis Group (Euronext:SAN; NYSE:SNY, Paris, France) markets Lovenox.

BioMarin Pharmaceutical Inc. (NASDAQ:BMRN), Novato, Calif.
Merck KGaA (Xetra:MRK), Darmstadt, Germany
Product: PEG-PAL (formerly Phenylase)
Business: Metabolic
Molecular target: NA
Description: Pegylated recombinant phenylalanine ammonia lyase (PAL) enzyme
Indication: Treat phenylketonuria (PKU)
Endpoint: Blood phenylalanine concentrations; safety, immune response and pharmacokinetics
Status: Preliminary Phase II data
Milestone: Phase II data (4Q10)

Preliminary data from an ongoing, open-label, dose-escalation, U.S. Phase II trial showed that 6 of 7 patients receiving at least 1 mg/kg/week

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subcutaneous PEG-PAL for at least 4 weeks had phenylalanine levels <600 $\mu\text{mol/L}$ for at least 3 weeks. Specifically, median phenylalanine levels were reduced to 527 $\mu\text{mol/L}$ from 1,293 $\mu\text{mol/L}$ at baseline and 2 patients achieved phenylalanine levels of <5 $\mu\text{mol/L}$. An additional 16 patients have been treated with lower PEG-PAL doses at shorter time periods and are continuing to have their doses escalated according to protocol. The most common treatment-related adverse event was injection site reactions.

Patients are receiving once-weekly subcutaneous PEG-PAL for 8 weeks at fixed doses starting at 0.001 mg/kg followed by 8 weeks of dose and frequency optimization. Patients will then receive escalating doses of up to 2 mg/kg/week PEG-PAL for at least 8 weeks in an extension study. Merck's Merck Serono S.A. unit has opt-in rights to PEG-PAL outside of the U.S. and Japan to treat PKU.

BioMarin Pharmaceutical Inc. (NASDAQ:BMRN), Novato, Calif.

Summit Corp. plc (LSE:SUMM), Abingdon, U.K.

Product: BMN 195 (formerly SMT C1100)

Business: Musculoskeletal

Molecular target: NA

Description: Small molecule utrophin up-regulator

Indication: Treat Duchenne muscular dystrophy (DMD)

Endpoint: Safety and pharmacokinetics

Status: Development discontinued

Milestone: NA

BioMarin discontinued development of BMN 195 after a double-blind, placebo-controlled, single and multiple dose-escalation Phase I trial in an undisclosed number of healthy volunteers showed that BMN 195 at doses of up to 400 mg/kg failed to achieve plasma concentrations that the company believed was required to increase utrophin expression. Furthermore, plasma concentrations of BMN 195 were even lower following repeat administration of the compound. As a result, BioMarin will terminate the partners' 2008 deal and return to Summit all rights for BMN 195 (see *BioCentury*, July 28, 2008 & June 8, 2009). BioMarin said it continues to believe that utrophin up-regulation is a viable approach to treat DMD. Summit said it believes that an "appropriate formulation" of BMN 195 can continue development, and it plans to seek a new partner to financially support the program.

Cardioxyl Pharmaceuticals Inc., Chapel Hill, N.C.

Product: CXL-1020

Business: Cardiovascular

Molecular target: Not available

Description: Small molecule nitroxyl (HNO) donor

Indication: Treat acute decompensated heart failure (ADHF)

Endpoint: Safety; pharmacokinetic and hemodynamic effects

Status: Phase I/IIa data

Milestone: NA

In a double-blind, placebo-controlled, dose-escalating, U.S. Phase I/IIa trial in 28 patients with chronic stable heart failure, IV CXL-1020 was well tolerated up to 10 $\mu\text{g/kg/minute}$ with no serious adverse events. CXL-1020 also displayed significant hemodynamic activity in patients with relevant underlying disease.

Excaliard Pharmaceuticals Inc., Carlsbad, Calif.

Isis Pharmaceuticals Inc. (NASDAQ:ISIS), Carlsbad, Calif.

Product: EXC 001

Business: Dermatology

Molecular target: NA

Description: Antisense compound that inhibits fibrosis

Indication: Treat scarring in patients undergoing abdominoplasty

Endpoint: Physician and patient assessment of healing and visual analog scales; safety

Status: Phase II data

Milestone: Final Phase II data (2H10)

In a double-blind, U.S. Phase II trial in an undisclosed number of patients undergoing elective abdominoplasty, intradermal injections of EXC 001 led to significant improvements in scarring in both physician and patient reported outcomes vs. placebo at week 12 post-surgery ($p \leq 0.017$). EXC 001 was well tolerated with no clinically important adverse events. Excaliard licensed EXC 001 from Isis in 2007 (see *BioCentury*, Dec. 3, 2007).

Ganymed Pharmaceuticals AG, Mainz, Germany

Product: Claudiximab (iMAB362)

Business: Cancer

Molecular target: CLND18.2

Description: Monoclonal antibody (mAb) targeting cell surface antigen CLND18.2

Indication: Treat gastroesophageal cancer

Endpoint: Maximum tolerated dose (MTD); safety, pharmacokinetics and overall tumor response

Status: Phase I data

Milestone: NA

In an open-label, single dose-escalation, German and Latvian Phase I trial in about 15 patients with gastroesophageal cancer, IV claudiximab was well tolerated up to 1 g/m² with no serious adverse events reported.

Genzyme Corp. (NASDAQ:GENZ), Cambridge, Mass.

Isis Pharmaceuticals Inc. (NASDAQ:ISIS), Carlsbad, Calif.

Product: Mipomersen (ISIS 301012 subcutaneous)

Business: Metabolic

Molecular target: Apolipoprotein B-100 (APOB-100) mRNA

Description: Second-generation antisense inhibitor of Apolipoprotein B-100 (APOB-100) mRNA

Indication: Treat high-risk hypercholesterolemia

Endpoint: Percent change in LDL-C from baseline to week 28; reductions in APOB, total cholesterol and non-HDL cholesterol

Status: Phase III data

Milestone: Submit MAA (IHI1); submit NDA (IHI1)

A double-blind, U.S. and Canadian Phase III trial in 158 patients with hypercholesterolemia and at high risk of developing coronary heart disease (CHD) showed that once-weekly subcutaneous injections of 200 mg mipomersen for 26 weeks met the primary endpoint of significantly reducing LDL-C from baseline to week 28 vs. placebo (37% vs. 5%, $p < 0.001$). Specifically, mipomersen reduced LDL-C from an average of 123 mg/dL at baseline to 75 mg/dL at week 28, with 50% of patients achieving LDL-C <70 mg/dL. Mipomersen also met the secondary endpoints of significantly reducing APOB, total cholesterol and non-HDL cholesterol vs. placebo ($p < 0.001$ for each). Patients were already receiving a maximally tolerated statin regimen.

Additionally, 26 patients receiving mipomersen and 2 patients receiving placebo discontinued treatment due to adverse events, including elevations in liver alanine transaminase (ALT) levels, injection-site reactions and flu-like symptoms. Specifically, 10% of patients treated with mipomersen had persistent ALT levels that were 3 times the upper limit of normal vs. an undisclosed percentage for placebo. The partners said the nature of the AEs were "generally similar" to what was seen in earlier trials. None of the patients had changes in other laboratory tests that would indicate hepatic dysfunction.

Genzyme plans to submit U.S. and EU regulatory applications in

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IH11 for mipomersen to treat homozygous familial hypercholesterolemia (hoFH). The partners said the applications may also include patients with severe hypercholesterolemia. Genzyme has exclusive rights to mipomersen from Isis (see *BioCentury*, Jan. 14, 2008; May 19, 2008; & June 30, 2008).

Indication: Treat severe hypercholesterolemia

Endpoint: Percent change in LDL-C from baseline to week 28; reductions in APOB, total cholesterol and non-HDL cholesterol

Status: Phase III data

Milestone: Submit MAA (IH11); submit NDA (IH11)

A double-blind, international Phase III trial in 58 patients with severe hypercholesterolemia showed that once-weekly subcutaneous injections of 200 mg mipomersen for 26 weeks met the primary endpoint of significantly reducing LDL-C from baseline to week 28 vs. placebo (36% reduction vs. 13% increase, $p < 0.001$). Specifically, mipomersen reduced LDL-C from an average of 276 mg/dL at baseline to 175 mg/dL at week 28. Mipomersen also met the secondary endpoints of significantly reducing APOB, total cholesterol and non-HDL cholesterol vs. placebo ($p < 0.001$ for each). Patients were already receiving maximally tolerated lipid-lowering medications.

Additionally, 8 patients receiving mipomersen and 1 patient receiving placebo discontinued treatment due to adverse events, including elevations in liver alanine transaminase (ALT) levels, injection-site reactions and flu-like symptoms. Specifically, 15% of patients treated with mipomersen had persistent ALT levels that were 3 times the upper limit of normal vs. an undisclosed percentage for placebo. The partners said the nature of the AEs were "generally similar" to what was seen in earlier trials. None of the patients had changes in other laboratory tests that would indicate hepatic dysfunction.

Genzyme plans to submit U.S. and EU regulatory applications in IH11 for mipomersen to treat homozygous familial hypercholesterolemia (hoFH). The partners said the applications may also include patients with severe hypercholesterolemia. Genzyme has exclusive rights to mipomersen from Isis (see *BioCentury*, Jan. 14, 2008; May 19, 2008; & June 30, 2008).

Hopital Necker-Enfants Malades, Paris, France, et al.

Product: Gamma-c gene therapy

Business: Hematology

Molecular target: NA

Description: *Ex vivo* gene therapy using autologous CD34+ cells transduced with a retroviral vector encoding the gamma-c cytokine receptor subunit

Indication: Treat X-linked severe combined immunodeficiency (SCID-X1)

Endpoint: Safety

Status: NA data

Milestone: NA

Researchers at the hospital and colleagues reported long-term follow-up data from 9 boys treated with *ex vivo* gamma-c gene therapy showing that 8 patients were alive at a median follow-up of 9 years. Four patients developed acute leukemia, 1 of whom died. Transduced T cells were detected for up to 10.7 years following the gene therapy. Seven patients had sustained immune reconstitution, 3 of whom required immunoglobulin-replacement therapy.

A tenth patient treated in Australia had insufficient T cell reconstitution and was given an allograft hematopoietic stem cell transplant 26 months after gene therapy. That patient died from fungal pneumonia 18 months after the allograft. Data were published in the *New England*

Journal of Medicine.

The researchers previously reported that 4 boys receiving the gene therapy showed evidence of a functional immune system with sustained clinical benefit for up to 2.5 years (see *BioCentury*, April 22, 2002). In 2002, FDA placed a hold on all active gene therapy trials using retroviral vectors to insert genetic material into blood stem cells after 2 patients developed leukemia in the trial (see *BioCentury*, Oct. 7, 2002 & Jan. 20, 2003). An FDA advisory committee advised the agency to remove the clinical hold in 2003.

Infinity Pharmaceuticals Inc. (NASDAQ:INFI), Cambridge, Mass.

Product: Retaspimycin (IPI-504)

Business: Cancer

Molecular target: Heat shock protein 90 (Hsp90)

Description: Small molecule Hsp90 inhibitor

Indication: Treat breast cancer

Endpoint: Overall response rate (ORR) and safety; progression-free survival (PFS), time to progression and overall survival (OS)

Status: Development discontinued

Milestone: Additional Phase II data (2011)

Infinity discontinued development of IPI-504 to treat breast cancer after an interim review of data from 26 HER2-positive metastatic breast cancer patients enrolled in the first cohort of an open-label Phase II trial showed that once-weekly 300 mg/m² IV IPI-504 plus Herceptin trastuzumab displayed clinical activity that was insufficient to continue the study. The company said it believes the insufficient activity was a result of the compound being administered at a less than optimal dose. The combination was well tolerated.

Infinity said it will continue to evaluate IPI-504 in 2 ongoing studies to treat advanced non-small cell lung cancer (NSCLC): IPI-504 alone in a Phase II trial and in combination with Taxotere docetaxel in a Phase Ib trial. The company does not plan to start any new trials at this time.

Last year, Infinity temporarily halted enrollment in the trial in order to amend the protocol, which the company said may include evaluating a different dose and/or the institution of additional pharmacokinetic and pharmacodynamic monitoring. The move followed the company's termination of the Phase III RING trial to treat refractory gastrointestinal stromal tumors (GIST) after a review of safety data from the trial showed a higher than anticipated mortality rate among patients receiving IPI-504 (see *BioCentury*, April 20, 2009 & May 11, 2009). In 2008, Infinity reacquired full rights to IPI-504 from AstraZeneca plc (LSE:AZN; NYSE:AZN, London, U.K.) (see *BioCentury*, Dec. 15, 2008).

Herceptin is marketed in the U.S. by Genentech Inc., a unit of Roche (SIX:ROG; OTCQX:RHHBY, Basel, Switzerland), and by Roche elsewhere. sanofi-aventis Group (Euronext:SAN; NYSE:SNY, Paris, France) markets Taxotere.

Innocoll Inc., Ashburn, Va.

Product: Gentamicin Surgical Implant

Business: Infectious

Molecular target: Not applicable

Description: Gentamicin surgical implant developed using CollaRx sponge membrane technology

Indication: Prevent surgical site infections

Endpoint: Total incidence of surgical wound infections (SWI) at day 60 post-surgery; postoperative hospital length of stay, proportion of patients with superficial incisional SWI, deep incisional SWI, organ space SWI and surgically treated SWI, pathogen/bacteriology and ASEPSIS score at 60 days post-surgery

Status: Phase III data

Milestone: NA

Researchers from the Duke Clinical Research Institute and col-

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leagues reported that the double-blind, multi-center, U.S. Phase III INN-SWI-002 trial in 602 patients undergoing open or laparoscopically assisted colorectal surgery showed that Innocoll's gentamicin-collagen sponge implant performed worse than no intervention on the primary and multiple secondary endpoints. On the primary endpoint, the sponge group had a significantly higher rate of surgical-site infections occurring within 60 days after surgery vs. no intervention (30% vs. 20.9%, $p=0.01$).

On secondary endpoints, patients in the sponge group had a significantly higher incidence of superficial surgical-site infection vs. no intervention (20.3% vs. 13.6%, $p=0.03$), and a non-significantly higher incidence of deep surgical-site infection (8.3% vs. 6%, $p=0.26$). Furthermore, a significantly greater proportion of patients in the sponge group visited an emergency room or surgeon's office due to wound-related signs or symptoms vs. no intervention (19.7% vs. 11%, $p=0.004$). Subjects received 2 sponge implants above the fascia at the time of surgical closure or no intervention in addition to standard care, which included prophylactic systemic antibiotics. Data were published in the *New England Journal of Medicine*.

Gentamicin sponge implants are approved for surgical implantation in 54 countries outside the U.S. and have Fast Track designation in the U.S. as an adjunct to systemic antibiotics to prevent surgical site infections in high-risk patients. Innocoll, which sponsored the study, acquired the implant from Schering-Plough Corp., which was acquired by Merck & Co. Inc. (NYSE:MRK, Whitehouse Station, N.J.). Baxter International Inc. (NYSE:BAX, Deerfield, Ill.) has exclusive marketing and distribution rights to gentamicin in the U.S. Baxter told BioCentury that it will work with Innocoll to determine next steps for the technology.

Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.

Product: Boceprevir (SCH 503034)

Business: Infectious

Molecular target: HCV NS3 protease

Description: Hepatitis C virus (HCV) NS3 protease inhibitor

Indication: Treat chronic HCV genotype I infection in treatment-naïve patients

Endpoint: Proportion of patients achieving a sustained virologic response (SVR) defined as undetectable HCV RNA levels 24 weeks after the end of treatment; early virologic response in patients who achieve an SVR

Status: Phase III data

Milestone: Additional Phase III data (4Q10); submit MAA (year end 2010); submit rolling NDA (year end 2010)

The double-blind, international Phase III HCV SPRINT-2 trial in 1,097 treatment-naïve patients with chronic HCV genotype I infection showed that both regimens of boceprevir plus PegIntron peginterferon alfa-2b and Rebetol ribavirin met the primary endpoint of a significantly greater proportion of patients achieving an SVR vs. placebo plus PegIntron and Rebetol. Specifically, 66% and 63% of patients in the 48-week and response-guided treatment groups achieved an SVR, respectively, vs. 38% for placebo plus PegIntron and Rebetol ($p<0.0001$ for both).

In non-African-American patients ($n=938$), 69% and 67% of patients in the 48-week and response-guided treatment groups achieved an SVR, respectively, vs. 40% for placebo plus PegIntron and Rebetol ($p<0.0001$ for both). In African-American patients ($n=159$), 53% and 42% of patients in the 48-week and response-guided treatment groups achieved an SVR, respectively, vs. 23% for placebo plus PegIntron and Rebetol ($p=0.004$ and $p=0.044$, respectively).

Patients in the 48-week treatment group received a 4-week lead in with 1.5 µg/kg/week PegIntron and 600-1,400 mg/day Rebetol, followed by the addition of thrice-daily 800 mg boceprevir for 44 weeks. Patients in the response-guided treatment group received a 4-week lead in with PegIntron and Rebetol, followed by the addition of boceprevir for 24 weeks. Patients with undetectable virus at week 8 and through week 24 stopped all treatment at week 28. Patients with detectable virus at week 8, but undetectable virus at week 24, stopped boceprevir treatment at week 28 and continued PegIntron and Rebetol for an additional 20 weeks. Merck markets PegIntron and Rebetol. Boceprevir has Fast Track designation in the U.S. for the indication.

Indication: Treat chronic HCV genotype I infection in patients who failed prior therapy

Endpoint: Proportion of patients achieving a sustained virologic response (SVR) defined as undetectable HCV RNA levels 24 weeks after the end of treatment; early virologic response in patients who achieve an SVR

Status: Phase III data

Milestone: Additional Phase III data (4Q10); submit MAA (year end 2010); submit rolling NDA (year end 2010)

The double-blind, international Phase III HCV RESPOND-2 trial in 403 patients with chronic HCV genotype I infection who failed prior therapy with peginterferon and ribavirin showed that both regimens of boceprevir plus PegIntron peginterferon alfa-2b and Rebetol ribavirin met the primary endpoint of a significantly greater proportion of patients achieving an SVR vs. placebo plus PegIntron and Rebetol. Specifically, 66% and 59% of patients in the 48-week and response-guided treatment groups achieved an SVR, respectively, vs. 21% for placebo plus PegIntron and Rebetol ($p<0.0001$ for both).

Patients in the 48-week treatment group received a 4-week lead in with 1.5 µg/kg/week PegIntron and 600-1,400 mg/day Rebetol, followed by the addition of thrice-daily 800 mg boceprevir for 44 weeks. Patients in the response-guided treatment group received a 4-week lead in with PegIntron and Rebetol, followed by the addition of boceprevir for 32 weeks. Patients with undetectable virus at weeks 8 and 12 stopped all treatment at week 36. Patients with detectable virus at week 8, but undetectable virus at week 12, stopped boceprevir treatment at week 36 and continued PegIntron and Rebetol for an additional 12 weeks. Merck markets PegIntron and Rebetol. Boceprevir has Fast Track designation in the U.S. for the indication.

Northwest Biotherapeutics Inc. (OTCBB:NWBO), Bethesda, Md.

Product: DCVax-Brain

Business: Cancer

Molecular target: Not applicable

Description: Autologous dendritic cells treated ex vivo with glioblastoma tumor fragments

Indication: Treat glioblastoma multiforme (GBM)

Endpoint: Overall survival (OS) and time to progression

Status: Updated Phase I/II data

Milestone: NA

Updated pooled data from 20 patients in U.S. Phase I and Phase I/II trials of DCVax-Brain plus standard of care (SOC) to treat newly-diagnosed GBM showed that no patients died from Oct. 1, 2009 through July 1, 2010. Overall, 5 (25%) patients were alive at July 1, with 33% and 27% of patients achieving 4- and ≥ 6 -year survival, respectively. Median OS was 3 years and the longest surviving patient to date has exceeded 10 years.

DCVax-Brain is approved in Switzerland for use at selected centers to treat malignant brain cancers, including GBM. The vaccine has Orphan Drug designation in the U.S. and EU. In its last survival update from Jan.

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I, 2009 through Sept. 30, 2009, the company reported that 1 patient died after surviving 80.5 months (see *BioCentury*, Oct. 26, 2009).

Oncimmune Ltd., Nottingham, U.K.

Proteome Sciences plc (LSE:PRM), Cobham, U.K.

Product: EarlyCDT-Lung

Business: Diagnostic

Molecular target: NA

Description: Autoantibody blood test against a panel of six tumor-related antigens

Indication: Detect early lung cancer

Endpoint: Sensitivity and specificity

Status: NA data

Milestone: NA

An international validation study in 3 cohorts of patients in the U.S. and Russia; Germany; and the U.S., U.K. and Ukraine, respectively, with newly diagnosed lung cancer (n=145, 241 and 269) showed that Oncimmune's EarlyCDT-Lung test had sensitivities of 36%, 39% and 37% and specificities of 91%, 89% and 90%, respectively. All patients in the first cohort were smokers. Additionally, there was no significant difference between different lung cancer stages detected by the test, which detected both small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Furthermore, the presence of benign lung disease did not affect the specificity of the test. Data were published in *Annals of Oncology*.

The autoantibody blood test against a panel of 6 tumor-related antigens — p53, cancer/testis antigen 1B (CTAG1B; NY-ESO-1), cancer/testis antigen (CAGE), tumor-associated antigen GBU4-5 (GBU4-5), annexin A1 (ANXA1) and SRY (sex determining region Y)-box 2 (SOX2) — is marketed in the U.S. to identify lung cancer in blood samples. Oncimmune licensed non-exclusive rights to the annexin biomarkers used in the test from Proteome Sciences.

Vicept Therapeutics Inc., Malvern, Pa.

Product: V-101

Business: Dermatology

Molecular target: Adrenergic receptor alpha

Description: Topical cream targeting alpha adrenergic receptors on small blood vessels

Indication: Treat erythema in patients with rosacea

Endpoint: Pharmacokinetics and pharmacodynamics

Status: Phase I data

Milestone: Start Phase II (3Q10)

Preliminary data from a double-blind, crossover, U.S. Phase I trial in 22 patients with rosacea showed that V-101 had a side effect profile similar to that of placebo and significantly improved moderate to severe erythema as measured by the Clinician's Erythema Assessment Scale and Subject Self Assessment Scale.

YM BioSciences Inc. (TSX:YM; NYSE-A:YMI), Mississauga, Ontario

Product: CYT387

Business: Cancer

Molecular target: Janus kinase-2 (JAK-2)

Description: Janus kinase-2 (JAK-2) inhibitor

Indication: Treat myelofibrosis

Endpoint: Safety, dose-limiting toxicity and maximum tolerated dose (MTD) (Phase I), and preliminary efficacy as measured by spleen size reduction by palpation and MRI (Phase II); pharmacodynamics, including myeloid colony formation and cytokine levels

Status: Phase I/II data

Milestone: Start pivotal trial (2011); Phase I/II data (12/2010)

In the dose-escalation Phase I portion of a Phase I/II trial in 21 patients, 100, 150, 200, 300 and 400 mg daily CYT387 for up to 9 months significantly reduced spleen size from baseline as measured by palpation. Reversible, dose-limiting toxicities of asymptomatic grade 3 amylase and lipase elevation and grade 3 headache were observed in 2 patients at the 400 mg CYT387 dose. Based on the results, YM said it will expand enrollment in the Phase II portion of the trial to 120 from 60 patients. The Phase II portion has currently enrolled 15 patients.

Earlier this year, an independent DSMB recommended expanding enrollment in the trial based on the observation of "favorable safety and biological activity data" (see *BioCentury*, April 5). YM plans to present data from the trial at the American Society of Hematology meeting in Orlando in December. YM acquired CYT387 through its acquisition of Cytopyia Ltd. (see *BioCentury*, Feb. 8).

PRECLINICAL RESULTS

Argos Therapeutics Inc., Durham, N.C.

Product: Dendritic cells electroporated with translationally enhanced IL-4 mRNA (eDC/IL-4)

Indication: Treat Type I diabetes

A significant proportion of non-obese diabetic mice receiving a single injection of dendritic cells electroporated with translationally enhanced IL-4 mRNA were able to maintain stable glycemia for several months after the onset of hyperglycemia compared to mice treated with saline or control electroporated dendritic cells. Data were published in *Molecular Therapy*.

DiaMedica Inc. (TSX-V:DMA), Winnipeg, Manitoba

Product: DM-99

Indication: Treat rheumatoid arthritis

In a collagen-induced animal model of RA, DM-99 significantly reduced joint swelling by up to 90% vs. control ($p < 0.001$). Furthermore, a single dose of the undisclosed naturally occurring protein that inhibits glycogen synthase kinase 3 (GSK3) beta administered at the first signs of RA symptoms delayed the onset and severity of disease, while treatment every fourth day completely halted the autoimmune attack. The company's DM-199, a recombinant version of DM-99, is in preclinical testing for diabetes and Alzheimer's disease.

Indication: Treat skin inflammation

In a delayed hypersensitivity model, a single dose of DM-99 significantly reduced skin inflammation by 67% vs. control ($p < 0.05$). Furthermore, skin inflammation following a single dose of the undisclosed naturally occurring protein that inhibits glycogen synthase kinase 3 (GSK3) beta could be prevented for up to 14 days. DM-99 also delayed skin graft rejection by several days vs. control ($p < 0.05$). The company's DM-199, a recombinant version of DM-99, is in preclinical testing for diabetes and Alzheimer's disease.

Indication: Treat Type I diabetes

In a mouse model of Type I diabetes, twice-daily DM-99 significantly reduced fasting plasma glucose (FPG) by 68% compared with untreated control mice at day 21 ($p = 0.05$). The undisclosed naturally occurring protein that inhibits glycogen synthase kinase 3 (GSK3) beta also non-significantly reduced total glucose. Final data, including insulin production and beta cell proliferation, are expected in summer 2010.

In a single-blinded, crossover Phase II trial in 40 Type II diabetics, DM-99 significantly reduced total blood glucose over 4 hours after a meal vs. placebo ($p = 0.032$). The company's DM-199, a recombinant version of DM-99, is in preclinical testing for diabetes and Alzheimer's disease.

See next page

Preclinical Results,
from previous page

FTA Bioscience LLC, Cleveland, Ohio

Pure Bioscience (NASDAQ:PURE), El Cajon, Calif.

Product: Silver dihydrogen citrate

Indication: Treat onychomycosis

In a guinea pig model of onychomycosis, twice-daily topical silver dihydrogen citrate for 7 days produced significant mycological and clinical improvements vs. untreated controls. FTA Bioscience has exclusive, worldwide rights to the electrolytically generated source of stabilized ionic silver from Pure Bioscience. FTA Bioscience plans to submit INDs for multiple silver dihydrogen citrate-based products to treat foot and nail funguses next year.

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.

Product: GSK299423

Indication: Treat antibiotic-resistant bacterial infections

In vitro, GSK299423 inhibited supercoiling by DNA gyrase from *Staphylococcus aureus* and *Escherichia coli* with IC50 values of 14 and 100 nM, respectively. Furthermore, the IC50 value for *E. Coli* DNA gyrase was not affected by the Ser83Leu mutation in the enzyme, which is associated with fluoroquinolone resistance. GSK299423 is a bacterial topoisomerase inhibitor that is structurally and mechanistically distinct from fluoroquinolones. Data were published in *Nature*.

PharmaGap Inc. (TSX-V:GAP), Ottawa, Ontario

Product: GAP-107B8

Indication: Treat cancer

In rats, single doses of IV GAP-107B8 administered at dose levels that produced peak plasma concentrations sufficient to kill cancer cells *in vitro* were well tolerated. Separately, PharmaGap said it has developed a bioanalytical method for measuring concentrations of the peptide therapeutic targeting protein kinase C (PKC) in plasma.

Virxsys Corp., Gaithersburg, Md.

Product: VRX1273

Indication: Treat and prevent HIV infection

In rhesus macaques, prophylactic VRX1273 improved immune responses and led to significant control of viral load over the 4 months following challenge with simian immunodeficiency virus (SIV) vs. unvaccinated controls. Additionally, there were no adverse reactions observed in any of the vaccinated animals following multiple infusions of VRX1273. Data were presented at the International AIDS Conference in Vienna. Virxsys plans to submit an IND for the lentiviral vector-based HIV vaccine by mid-2011.

CLINICAL STATUS

Acceleron Pharma Inc., Cambridge, Mass.

Celgene Corp. (NASDAQ:CELG), Summit, N.J.

Product: ACE-011

Business: Hematology

Molecular target: Activin receptor type 2a (ACVR2A)

Description: Activin receptor type 2A antagonist

Indication: Treat renal anemia

Endpoint: Single-dose pharmacokinetics, proportion of patients achieving an increase in Hb \geq 1 g/dL during any 4-week period; adverse events, proportion of patients with Hb $>$ 12 g/dL, proportion of patients with rise in Hb $>$ 2 g/dL during a 4-week period and blood pressure changes from baseline

Status: Phase IIa started

Milestone: NA

Celgene began a 2-part, double-blind Phase IIa (REN-001) trial in 32 patients. The first part will compare a single 0.1 mg/kg subcutaneous dose of ACE-011 vs. placebo in 8 patients. The second part will evaluate multiple doses of ACE-011 vs. an erythropoiesis-stimulating agent (ESA) in 24 patients. Acceleron and Celgene are co-developing ACE-011 under a 2008 deal (see *BioCentury*, Feb. 25, 2008).

Access Pharmaceuticals Inc. (OTCBB:ACCP), Dallas, Texas

Product: Thiarabine T-araC

Business: Cancer

Molecular target: NA

Description: Nucleoside analog

Indication: Treat hematological malignancies

Endpoint: Safety and maximum tolerated dose (MTD); reduction in blast cells

Status: Phase I/II started

Milestone: Complete Phase I/II enrollment (1Q11); Phase I/II data (2Q11)

Access Pharmaceuticals began an open-label, dose-escalation, U.S. Phase I/II trial to evaluate 4 dose strengths of thiarabine given once daily for 3 or 5 days in up to 70 patients.

Aeterna Zentaris Inc. (TSX:AEZ; NASDAQ:AEZS), Quebec City, Quebec

Product: AEZS-108 (formerly AN-152, ZEN-008)

Business: Cancer

Molecular target: GnRH/LHRH receptor

Description: Doxorubicin chemotherapeutic conjugated to luteinizing hormone-releasing hormone (LHRH) receptor agonist

Indication: Treat castration- and taxane-resistant metastatic prostate cancer

Endpoint: NA

Status: Phase I/II start

Milestone: Start Phase I/II (year end 2010)

By year end, researchers will begin a dose-escalation, U.S. Phase I/II trial to evaluate intravenous AEZS-108 in about 55 patients. The study will be supported by a grant from NIH.

Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan

Product: AGS-8M4, ASP6183

Business: Cancer

Molecular target: NA

Description: Antibody against chondrolectin

Indication: Treat ovarian cancer

Endpoint: NA

Status: Phase II discontinued

Milestone: NA

Astellas said it suspended U.S. Phase II testing of ASP6183 to treat ovarian cancer after a review of new and existing preclinical data. Additional details were not disclosed.

Bio-Path Holdings Inc. (Pink:BPTH), Ogden, Utah

Product: Liposomal Grb-2 (BP-100-1.01)

Business: Cancer

Molecular target: Growth factor receptor-bound protein 2 (GRB2)

Description: Liposomal antisense inhibitor of growth factor receptor-bound protein 2 (GRB2) expression

Indication: Treat hematological malignancies

Endpoint: Pharmacokinetics and safety

Status: Phase I started

Milestone: NA

Bio-Path began a dose-escalation, U.S. Phase I trial to evaluate 5 dose levels of Liposomal Grb-2 in 18-30 patients.

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Clinical Status,
from previous page

Biovail Corp. (TSX:BVF; NYSE:BVF), Mississauga, Ontario

Product: BVF-324

Business: Genitourinary

Molecular target: NA

Description: Tramadol

Indication: Treat premature ejaculation

Endpoint: NA

Status: Phase III discontinued

Milestone: NA

Biovail said it discontinued development of BVF-324 to treat premature ejaculation due to slow enrollment in Phase III trials and after a reevaluation of the product's commercial potential. The company acquired exclusive, worldwide rights to the tramadol formulation from an undisclosed party in 2007.

Boston Scientific Corp. (NYSE:BSX), Natick, Mass.

Product: Synergy stent

Business: Cardiovascular

Molecular target: NA

Description: Bioabsorbable everolimus-eluting stent

Indication: Treat coronary artery lesions

Endpoint: Non-inferiority to Promus Element on target lesion failure at 30 days and a composite measure of cardiac death, myocardial infarction and target lesion

Status: NA started

Milestone: Data (year end 2011 - early 2012)

Boston Scientific began the single-blind, international pivotal EVOLVE trial to evaluate Synergy stent vs. Promus Element everolimus-eluting stent in 291 patients. The company, which markets Promus Element, said data would be used to support CE Mark approval of Synergy stent.

Celgene Corp. (NASDAQ:CELG), Summit, N.J.

Product: Apremilast (CC-10004)

Business: Autoimmune

Molecular target: Phosphodiesterase-4 (PDE-4); Interleukin-2 (IL-2)

Description: Anti-inflammatory molecule that inhibits phosphodiesterase-4 (PDE-4), tumor necrosis factor (TNF) alpha, interleukin-2 (IL-2) and nitric oxide synthase (NOS)

Indication: Treat psoriatic arthritis

Endpoint: Proportion of patients achieving a 20% improvement in the American College of Rheumatology criteria (ACR20) at 24 weeks; physical function and durability of ACR20 response at 52 weeks

Status: Phase III started

Milestone: NA

Celgene began a double-blind, placebo-controlled Phase III (PSA-002) trial to evaluate 20 or 30 mg apremilast given twice daily in 495 patients.

Product: Revlimid lenalidomide (formerly CDC 501)

Business: Cancer

Molecular target: Unknown

Description: Thalidomide analog

Indication: Treat diffuse large B cell lymphoma (DLBCL)

Endpoint: Response rate

Status: Phase II/III started

Milestone: NA

Celgene began a double-blind Phase II/III (DLC-001) trial to compare Revlimid vs. a single agent of investigator's choosing. The Phase II

portion will stratify 100 patients by non-germinal center B cell (GCB) or GCB phenotype.

Cell Therapeutics Inc. (NASDAQ:CTIC; Milan:CTIC), Seattle, Wash.

Product: Pixuvri pixantrone

Business: Cancer

Molecular target: Topoisomerase II (TOP2)

Description: Aza-anthracedione DNA intercalating agent that inhibits topoisomerase II (TOP2)

Indication: Treat relapsed/refractory aggressive B-cell non-Hodgkin's lymphoma (NHL) in patients who failed first- to third-line regimens and are ineligible for transplant

Endpoint: Response rate, progression-free survival (PFS) and overall survival (OS)

Status: SPA submitted

Milestone: Start Phase III (2010)

Cell Therapeutics submitted an SPA to FDA for a proposed Phase III trial designed to compare pixantrone plus Rituxan rituximab against current standard regimens. The company hopes to start the trial this year.

Celldex Therapeutics Inc. (NASDAQ:CLDX), Needham, Mass.

Product: CDX-011 (formerly CR011-vcMMAE)

Business: Cancer

Molecular target: Glycoprotein NMB (GPNMB); Tubulin

Description: Human monoclonal antibody (mAb) against glycoprotein NMB (GPNMB) linked to tubulin inhibitor monomethyl auristatin E (MMAE)

Indication: Treat advanced, refractory/resistant GPNMB-expressing breast cancer

Endpoint: NA

Status: Phase IIb start

Milestone: Start Phase IIb (3Q10)

This quarter, Celldex will begin a Phase IIb trial in 120 patients to compare 1.88 mg/kg intravenous CDX-011 given on day 1 of each 21-day cycle vs. single agent chemotherapeutic of investigator's choosing. CDX-011 has Fast Track designation in the U.S.

Galapagos N.V. (Euronext:GLPG; Pink:GLPYY), Mechelen, Belgium

Product: GLPG0634

Business: Autoimmune

Molecular target: Janus kinase-1 (JAK-1); Janus kinase-2 (JAK-2)

Description: JAK-1 and JAK-2 inhibitor

Indication: Treat arthritis

Endpoint: Safety, pharmacokinetics and pharmacodynamics

Status: Phase I start

Milestone: NA

This week, Galapagos will begin a double-blind, placebo-controlled, Belgian Phase I trial to evaluate single and multiple ascending doses of oral GLPG0634 in at least 40 healthy volunteers. Last week, Galapagos acquired full rights to the compound from GlaxoSmithKline plc (LSE:GSK; NYSE:GSK, London, U.K.) which had an option under an ongoing 2006 deal to license the arthritis candidate after Phase IIa testing (see *BioCentury*, July 12, 2006 & July 16, 2007).

Living Cell Technologies Ltd. (ASX:LCT; OTCQX:LVCLY), Sydney, Australia

Product: DiabeCell

Business: Endocrine

Molecular target: Not available

Description: Encapsulated porcine pancreatic islet cells

Indication: Treat Type I diabetes

See next page

Clinical Status,
from previous page

Endpoint: Safety and reduction in HbA1c levels; improvement in glucose lability, reduction in hypoglycemia, reduction in insulin dose, improvement in endogenous insulin secretion and improvement in quality of life
Status: Phase II expanded
Milestone: NA

Living Cell received approval to expand enrollment to 12 patients from 8 in an ongoing dose-ranging, New Zealand Phase II trial evaluating Diabecell implants.

N30 Pharma LLC, Boulder, Colo.

Product: N6022

Business: Inflammation

Molecular target: S-nitrosoglutathione reductase

Description: Selective and reversible inhibitor of S-nitrosoglutathione reductase (GSNOR)

Indication: Treat asthma, chronic obstructive pulmonary disease (COPD) and inflammatory bowel disease (IBD)

Endpoint: Safety and pharmacokinetics

Status: Phase I start

Milestone: Start Phase I (09/2010)

Next month, N30 Pharma will begin a dose-escalation Phase I trial to evaluate single intravenous doses of N6022 in healthy volunteers.

Neurocrine Biosciences Inc. (NASDAQ:NBIX), San Diego, Calif.

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.

Product: 561679

Business: Neurology

Molecular target: Corticotropin-releasing factor receptor 1 (CRHR1) (CRFRI)

Description: Corticotropin-releasing factor (CRF) receptor 1 antagonist

Indication: Treat women with post-traumatic stress disorder

Endpoint: Clinician-Administered PTSD scale (CAPS) after 6 weeks of treatment; Montgomery-Asberg Depression Rating Scale (MADRS)

Status: Phase II started

Milestone: NA

Neurocrine disclosed in its earnings that partner GlaxoSmithKline began a double-blind, placebo-controlled Phase II trial to evaluate oral 561679 in about 150 patients. The companies are developing CRF antagonists under a 2001 deal (see *BioCentury*, July 30, 2001).

Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland

Product: Undisclosed HuCAL antibody for ophthalmology

Business: Ophthalmic

Molecular target: NA

Description: Undisclosed antibody developed using MorphoSys' HuCAL GOLD library

Indication: Treat ophthalmic disease

Endpoint: NA

Status: Phase I started

Milestone: NA

Novartis began a Phase I trial of an undisclosed HuCAL antibody. The start triggers an undisclosed milestone payment to MorphoSys, which is using its HuCAL GOLD technology to discover and optimize antibodies against targets selected by Novartis under a 2007 deal that was expanded last year (see *BioCentury*, July 13, 2009).

Patrys Ltd. (ASX:PAB), Melbourne, Australia

Product: PAT-SM6

Business: Cancer

Molecular target: Heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa) (HSPA5) (GRP78)

Description: Human antibody that binds heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa; HSPA5; GRP78) and imports low-density lipoprotein (LDL) into cancer cells

Indication: Treat melanoma

Endpoint: Safety; pharmacokinetics, immunogenicity, anti-tumor activity, pharmacodynamics and biomarkers

Status: Phase I started

Milestone: NA

Patrys began an open-label, dose-escalation, Australian Phase I trial to evaluate IV PAT-SM6 in about 10 patients.

Pozen Inc. (NASDAQ:POZN), Chapel Hill, N.C.

Product: PA32540

Business: Cardiovascular

Molecular target: H+/K ATPase pump

Description: Tablet containing 325 mg aspirin core surrounded by an immediate-release coating of 40 mg omeprazole, a proton pump inhibitor (PPI)

Indication: Secondary prevention of cardio- and cerebrovascular events in patients at risk for developing aspirin-associated gastric ulcers

Endpoint: Long-term safety

Status: Completed Phase III enrollment

Milestone: Phase III data (2H11); submit NDA (2012)

Pozen completed enrollment of 380 patients in an open-label Phase III trial evaluating once-daily PA32540.

UCB Group (Euronext:UCB), Brussels, Belgium

Product: Vimpat lacosamide

Business: Neurology

Molecular target: Collapsin response mediator protein-2 (DPYSL2) (CRMP-2)

Description: Anticonvulsant that selectively enhances slow inactivation of sodium (Na) channels and modulates collapsin response mediator protein-2 (CRMP-2)

Indication: Treat primary generalized tonic-clonic seizures (PGTCS)

Endpoint: NA

Status: Phase II started

Milestone: Phase II data (2H11)

UCB began a U.S. and European Phase II trial to evaluate Vimpat lacosamide in patients.

ZymoGenetics Inc. (NASDAQ:ZGEN), Seattle, Wash.

Product: Interleukin-21 (IL-21)

Business: Cancer

Molecular target: Interleukin-21 (IL-21) receptor

Description: Recombinant interleukin-21 (IL-21)

Indication: Treat metastatic melanoma

Endpoint: Median progression-free survival (PFS); response rate and overall survival

Status: Phase IIb started

Milestone: NA

ZymoGenetics reported in its earnings that in June it began an open-label, Canadian Phase IIb trial to compare IL-21 vs. dacarbazine.

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OFFERINGS & SECURITIES TRANSACTIONS

Week ended 8/6/10. Shares after offering refers to shares outstanding. Proceeds are gross, not net. Shares offered don't include overallocments. Currency rates used in the week: A\$=US\$0.913; C\$=US\$0.9777; €=\$1.3072; £=\$1.5795

Completed Offerings

Alexza Pharmaceuticals Inc. (NASDAQ:ALXA), Mountain View, Calif.

Business: Drug delivery, Neurology

Date completed: 8/5/10

Type: Direct public offering

Raised: \$18 million

Units: 6.7 million

Price: \$2.70 (unit)

Shares after offering: 59.6 million

Placement agents: RBC Capital Markets; JMP Securities

Investors: Institutional investors

Note: Each unit comprises a share and a five-year warrant to purchase 0.5 shares, with each whole warrant exercisable at \$3.30.

Bradmer Pharmaceuticals Inc. (TSX:BMR), Toronto, Ontario

Business: Cancer

Date completed: 7/29/10

Type: Private placement

Raised: C\$499,999 (US\$488,849)

Shares: 5.3 million

Price: C\$0.10

Shares after offering: 19.7 million

Gemin X Pharmaceuticals Inc., Malvern, Pa.

Business: Cancer

Date completed: 8/4/10

Type: Venture financing

Raised: \$8 million

Investors: Caxton Advantage Life Sciences Fund; Sanderling; existing investors

Note: The company said all existing investors participated.

Helix BioPharma Corp. (TSX:HBP; Xetra:HBP), Aurora, Ontario

Business: Cancer, Drug delivery, Proteomics

Date completed: 8/6/10

Type: Private placement of units

Raised: C\$11 million (US\$10.8

million)

Units: 4.5 million

Price: C\$2.43 (unit)

Shares after offering: 64.4 million

Investor: Individual investor

Note: Each unit comprises a share and a three-year warrant to purchase a share at C\$3.40.

Idera Pharmaceuticals Inc. (NASDAQ:IDRA), Cambridge, Mass.

Business: Cancer, Infectious, Autoimmune

Date completed: 8/3/10

Type: Direct public offering

Raised: \$15.1 million

Units: 4.1 million

Price: \$3.71 (unit)

Shares after offering: 27.6 million

Placement agent: Rodman

Investors: Institutional investors

Note: Each unit comprises a share and a five-year warrant to purchase 0.4 shares, with each whole warrant exercisable at \$3.71.

NuPathe Inc. (NASDAQ:PATH), Conshohocken, Pa.

Business: Neurology

Date completed: 8/6/10

Type: IPO

Raised: \$50 million

Shares: 5 million

Price: \$10

Shares after offering: 14.5 million

Underwriters: Leerink; Lazard; Needham; Needham

Overallocment: 750,000

Note: Last week, NuPathe amended its IPO to drop Stifel Nicolaus Weisel as an underwriter.

Sareum Holdings plc (LSE:SAR), Cambridge, U.K.

Business: Supply/Service, Computational chemistry/biology, High throughput screening

Date completed: 8/3/10

Type: Private placement

Raised: £200,000 (\$315,900)

Shares: 100 million

Price: 0.2p

Shares after offering: 1.3 billion

Placement agent: Hybridan

Investors: Institutional investor

Trius Therapeutics Inc. (NASDAQ:TSRX), San Diego, Calif.

Business: Infectious

Date completed: 8/3/10

Type: IPO

Raised: \$50 million

Shares: 10 million

Price: \$5

Shares after offering: 23.6 million

Underwriters: Citigroup; Piper Jaffray; Canaccord; JMP Securities

Overallocment: 750,000

Note: Trius temporarily delayed the IPO in March until it could modify the protocol for the torezolid trial to conform to draft guidance on non-inferiority (NI) trials. Torezolid is a second-generation oxazolidinone, a bacterial protein biosynthesis inhibitor.

Wilex AG (Xetra:WL6), Munich, Germany

Business: Cancer

Date completed: 8/4/10

Type: Rights offering

Raised: €10.1 million (\$13.2 million)

Shares: 2.5 million

Price: €4.10

Shares after offering: 18.4 million

Investors: Existing investors

Note: Shareholders were eligible to purchase two shares for every 13 held. Shareholders dievini Hopp BioTech holding GmbH & Co. KG and UCB Group (Euronext:UCB, Brussels, Belgium) participated.

Proposed Offerings

Arena Pharmaceuticals Inc. (NASDAQ:ARNA), San Diego, Calif.

Business: Endocrine, Neurology, Cardiovascular

Date announced: 8/6/10

Type: Direct public offering

To be raised: \$60 million

Shares: 9 million

Price: \$6.70

Shares outstanding prior: 112.3 million

Investor: Deerfield Management

Note: Arena said it will use \$30 million of the proceeds to repay a portion of a \$100 million loan from Deerfield issued in June 2009. The loan bears 7.75% interest. Arena and Deerfield also amended the loan to defer the \$20 million

principal repayment due in July 2011 to June 17, 2012, subject to Arena receiving FDA approval for an NDA for lorcaserin for weight management by July 2011. The serotonin (5-HT2C) receptor agonist has an Oct. 22 PDUFA date.

Biofrontera AG (Xetra:B8F), Leverkusen, Germany

Business: Dermatology

Date announced: 8/4/10

Type: Rights offering

To be raised: Up to €7.9 million (\$10.3 million)

Shares: 3.6 million

Price: €2.20

Placement agent: Lang & Schwarz Broker

Shares outstanding prior: 9 million

Note: Shareholders are eligible to purchase two shares for every five held.

Biohit Oyj (HSE:BIIOBV), Helsinki, Finland

Business: Diagnostic

Date announced: 8/3/10

Type: Convertible bond financing

To be raised: €4.1 million (\$5.3 million)

Placement agent: Pohjola Corporate Finance

Shares outstanding prior: 10 million

Investors: Institutional investors

Note: The five-year bond bears 6.5% interest. The company expects to issue the bond Oct. 28.

Complete Genomics Inc., Mountain View, Calif.

Business: Genomics, Supply/Service

Date announced: 7/30/10

Type: IPO

To be raised: Up to \$86.3 million

Shares: TBD

Price: TBD

Underwriters: UBS; Jefferies; Baird; Cowen

Horizon Pharma Inc., Northbrook, Ill.

Business: Neurology, Inflammation, Autoimmune

Date announced: 8/3/10

See next page

***Proposed Offerings,
from previous page***

Type: IPO
To be raised: Up to \$86.3 million
Shares: TBD
Price: TBD
Underwriters: Jefferies; Piper Jaffray; JMP Securities; Lazard

Other Financial News

Aradigm Corp. (OTCBB: ARDM), Hayward, Calif.
Business: Drug delivery
Date announced: 8/2/10

Aradigm plans to exchange about \$9.1 million in an outstanding 5% promissory note issued to Novo Nordisk A/S (CSE:NVO; NYSE:NVO, Bagsvaerd, Denmark) for 26 million shares at \$0.35. The closing of the deal is subject to Aradigm shareholder approval.

Cardioxyl Pharmaceuticals Inc., Chapel Hill, N.C.
Business: Cardiovascular
Date announced: 8/2/10

Cardioxyl raised \$15 million in an extension of a series A round. Existing investors Aurora Funds and New Enterprise Associates co-led the round. Cardioxyl raised

\$14.5 million in the round in December 2006. The total amount raised in the round was undisclosed.

Genta Inc. (OTCBB:GETAD), Berkeley Heights, N.J.
Business: Cancer
Date announced: 7/30/10

Genta implemented a 1-for-100 reverse stock split effective Aug. 2 and began trading under the symbol "GETAD." Following the split, the company will have 8.4 million shares outstanding.

KV Pharmaceutical Co. (NYSE:KVA), St. Louis, Mo.
Business: Drug delivery, Generics
Date announced: 8/2/10

KV received a letter from NYSE indicating the company is not in compliance with the \$1 minimum bid price requirement for continued listing. The company has until Jan. 27, 2011 to regain compliance.

Marina Biotech Inc. (NASDAQ: MRNAD), Bothell, Wash.
Business: Cancer, Metabolic
Date announced: 8/2/10

Marina Biotech filed a shelf registration covering the sale of up to \$50 million of its securities.

Marina Biotech, which closed Friday at \$2.67, has 23.5 million shares outstanding.

Molecular Insight Pharmaceuticals Inc. (NASDAQ:MIPI), Cambridge, Mass.
Business: Diagnostic, Cancer
Date announced: 8/2/10

Molecular Insight said holders of outstanding senior secured bonds due 2012 agreed to extend for a sixth time a waiver of default for the bonds to Aug. 16.

MolMed S.p.A. (Milan:MLM), Milan, Italy
Business: Cancer
Date announced: 8/2/10

MolMed sold an additional 2.1 million shares in its July rights offering, raising an additional €1.1 million (\$1.5 million) and bringing the total raised in the offering to €57.9 million (\$74.7 million). Underwriters Jefferies and Banca IMI purchased 1.8 million shares.

Neoprobe Corp. (OTCBB: NEOP), Dublin, Ohio
Business: Diagnostic
Date announced: 8/3/10

Neoprobe filed a shelf registration covering the sale of up to \$20 million of its securities. Neoprobe,

which closed Friday at \$2.01, has 82.3 million shares outstanding.

Patrys Ltd. (ASX:PAB), Melbourne, Australia
Business: Antibodies, Cancer
Date announced: 8/3/10

Patrys secured a three-year funding facility for up to A\$15 million (US\$13.7 million) with Advance Opportunities Fund.

PDL BioPharma Inc. (NASDAQ: PDLI), Incline Village, Nev.
Business: Antibodies
Date announced: 8/5/10

PDL BioPharma converted \$61.6 million outstanding in 2.75% convertible notes due August 2023 into 11.1 million shares at \$5.55. PDL BioPharma said \$54.3 million in principal amount of the notes remain outstanding.

PharmAthene Inc. (NYSE-A: PIP), Annapolis, Md.
Business: Infectious
Date announced: 7/30/10

PharmAthene received notice from NYSE Amex indicating that the company is not in compliance with requirements for continued listing. The company said it expects to submit a plan to regain compliance.