

*Bridging the Valley of Death*

## Product Development Corporations Share Risks, Gain Popularity

By Brian Orelli

*BioWorld Insight* Contributing Writer

More products, but not more companies, has long been a rallying cry in biotech.

Company formation is not capital efficient, hence the rise of the virtual business model. But an increasing number of organizations are now experimenting with the hypothesis that if virtual is good, no company at all would be even better. They are middle-men: combing through a large number of early stage projects, advancing the best, and then handing them off to a partner. That used to be the very definition of a venture capitalist, and even of biotech itself, but as times have changed, new business models have arisen to fill the gap.

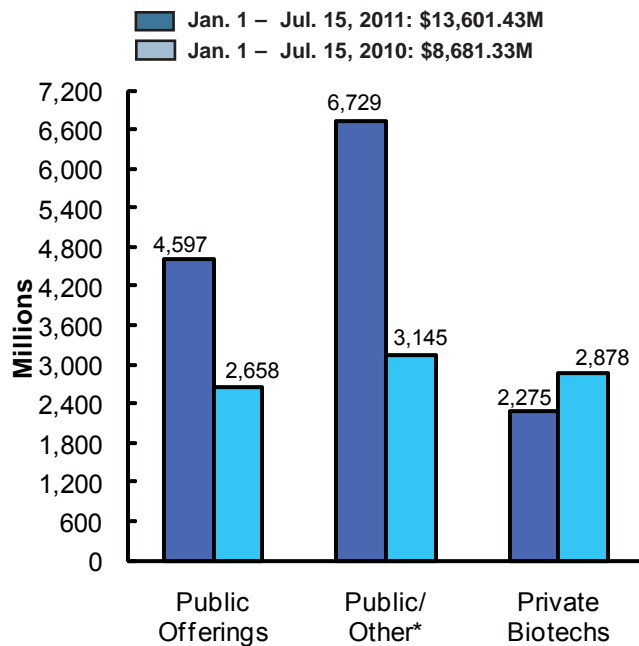
"It's a bit of push and pull," said Bruce Booth, partner at Atlas Ventures. A weak public market has pushed venture-backed companies towards pharma for exits. On the pull side, the cost-sensitive industry structure is demanding the outsourcing of development.

"There's an incredible supply out there," Booth said, pointing to both academic institutions with preclinical molecules as well as pharma-owned assets that they don't want to develop further. And plenty of organizations are looking for new ways to shepherd that supply across the "valley of death."

Whether the entities are called product development companies, product definition companies, asset-based funds, or something else, they're certainly not a new concept in the industry. For years, clinical research organizations (CRO) have taken stakes in start-ups in exchange for discounts on their services.

Calvert Research LLC, the investment arm of Calvert

### Money Raised By Biotech In 2011 Vs. 2010



\* Includes financings of public biotech firms with the exceptions of public offerings and certain investments from corporate partners.

Holdings, has backed companies with preclinical molecules for more than seven years. In addition to funding the investments with its cash flow, its CRO, Calvert Labs, helps determine which molecules to fund. (See *BioWorld Today*, Aug. 3, 2005.)

"We rely on the staff of our preclinical testing company and their experience to give us a good idea of how they think these compounds are going to react in animals," said Andy

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*Et tu, Actos?*

## Diabetes Prevention and the Problem with PPAR-Gamma

By **Trista Morrison**  
Editor

Last week, French regulators asked Takeda Pharmaceutical Co. Ltd. to pull diabetes drug Actos (pioglitazone) off the market – a move diabetes experts hope doesn't indicate Actos is starting down the same slippery slope as GlaxoSmithKline plc's Avandia (rosiglitazone).

Actos and Avandia are the only drugs that address the underlying cause of diabetes, according to Jerry Colca, president and chief scientific officer at Metabolic Solutions Development Co. (MSDC). Everything else – even the newer DPP-4 inhibitors and GLP-1 agonists – “only affects the symptoms,” Colca told *BioWorld Insight*.

The biopharma industry is still reeling from Avandia's downfall. After a 2007 *New England Journal of Medicine* article linked the drug to an increased risk of myocardial infarction, the FDA issued guidance requiring large cardiovascular safety studies for all new diabetes drugs. Those requirements essentially put diabetes out of the reach of many small biotechs, contributing to the demise of firms like Phenomix Corp. (See *BioWorld Today*, July 3, 2008, and *BioWorld Insight*, Nov. 15, 2010.)

Last fall, Avandia and other rosiglitazone-containing products were removed from the market in Europe. The FDA restricted access to the drugs, and Avandia sales fell from \$1.2 billion in 2009 to \$689.5 million in 2010. (See *BioWorld Today*, Sept. 24, 2010.)

Ironically, part of the rationale in restricting Avandia's use was that patients could always use Actos instead, as both drugs are thiazolidinediones and Actos has shown a better cardiovascular profile. But even back then, the FDA had concerns about increased bladder cancer risk with Actos, and last month an interim analysis from an ongoing epidemiological study prompted the agency to slap Actos with a bladder cancer warning label. (See *BioWorld Today*,

June 17, 2011.)

Now France has withdrawn Actos and the pioglitazone-containing product Competact from the market. A review by the European Medicine Agency's Committee for Medicinal Products for Human Use is ongoing and will be discussed at a meeting later this month.

The possibility that two blockbuster drugs, both staples of diabetes care for more than a decade, may be relegated to the margins is astounding. Colca said he can't imagine

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*(Dis)Incentives*

## Despite SGEN, Analysts Wary Of Accelerated Approval Path

By Trista Morrison  
Editor

Betting the future of Adcetris (brentuximab vedotin) on one single-arm Phase II trial in each of its two target indications paid off for Seattle Genetics Inc., which last week gained unanimous Oncologic Drugs Advisory Committee (ODAC) backing for accelerated approval in Hodgkin lymphoma and systemic anaplastic large cell lymphoma (ALCL). (See *BioWorld Today*, July 13, 2011, and July 15, 2011.)

But analysts fear the strategy might not work for other drugs seeking accelerated approval, including Onyx Pharmaceuticals Inc.'s carfilzombib.

The difference between success and failure in the accelerated approval arena appears to hinge on two factors: the degree of unmet need and the magnitude of benefit. That was the message ODAC gave at a February meeting on the topic, in which it maintained that randomized, controlled trials should remain the standard for accelerated approval.

The Adcetris decision falls right into step with ODAC's party line. Hodgkin lymphoma hasn't seen a new treatment in more than 30 years, and Adcetris garnered a 75 percent objective response rate and a 32 percent complete remission rate in its Phase II trial. Chemotherapy is also still the standard in ALCL, where Adcetris produced an 86 percent objective response rate and 53 percent complete remission rate.

Robert W. Baird & Co. analyst Christopher Raymond wrote in a recent report that "significant dissimilarities" exist between Adcetris and Onyx's carfilzombib.

In the unmet need category, carfilzombib is being developed for multiple myeloma, and while there's a significant unmet need for relapsed/refractory patients, Raymond noted that "other options do exist," including retreatment with Velcade (bortezomib, Millennium/Takeda Pharmaceutical Co. Ltd.).

When it comes to magnitude of benefit, carfilzombib's response rate of 24 months isn't as impressive as the numbers Adcetris threw up – though it bears noting Onyx's drug was tested in multiple myeloma patients who had failed an average of 13 previous drugs and usually have a response rate of about 11 percent.

Another firm eyeing accelerated approval based on a single-arm Phase II study is Ambit Biosciences Inc. with AC220 in acute myeloid leukemia (AML). Data are expected later this year, and Ambit and partner Astellas Pharma Inc. have said they hope those data are sufficient for approval.

In Ambit's case, the magnitude of benefit remains to be seen, but the unmet need does not bode well for the company. When the FDA rejected accelerated approval of Genzyme Corp.'s Clolar (clofarabine) and Vion Pharmaceuticals Inc.'s Onrigin (laromustine) in elderly AML, both based on single-arm Phase II trials, FDA cancer drug czar Richard Pazdur said

he has repeatedly emphasized the need for randomized trials in AML. (See *BioWorld Insight*, Sept. 7, 2009.)

His message resonated loud and clear with Cyclacel Pharmaceuticals Inc. After completing a Phase II study with AML drug sapacitabine, the firm decided to conduct a three-arm pivotal Phase III trial, which kicked off early this year.

Ditto for Sunesis Pharmaceuticals Inc. The biotech opted not to attempt accelerated approval for AML drug vosaroxin, despite good results in two separate Phase II trials. It began Phase III trials instead. (See *BioWorld Today*, Dec. 22, 2010.)

In the multiple myeloma space, Celgene Corp. is not necessarily betting on a single-arm trial to gain accelerated approval of pomalidomide, either. Recent Phase II data showed the drug plus low-dose dexamethasone generated an overall response rate of 42 percent after 21 days, but Celgene moved the drug into Phase III. Spokesman Greg Geissman said that while Celgene is "in discussions with the agency that include the potential for an accelerated filing . . . we are conducting a Phase III study because that is the normal path to approval."

Perhaps no FDA decision relating to accelerated approval has sparked more debate within the drug industry than the agency's refusal to even review Roche AG's and ImmunoGen Inc.'s breast cancer drug trastuzumab-DM1 (T-DM1) under the accelerated approval pathway. While a single-arm Phase II trial had shown a 33 percent response rate, and refractory HER2-positive breast cancer represents a clear unmet need, there was disagreement between the agency and the companies regarding what, exactly, constitutes a refractory HER2-positive breast cancer patient. Phase III trials are now underway. (See *BioWorld Insight*, Sept. 27, 2010.)

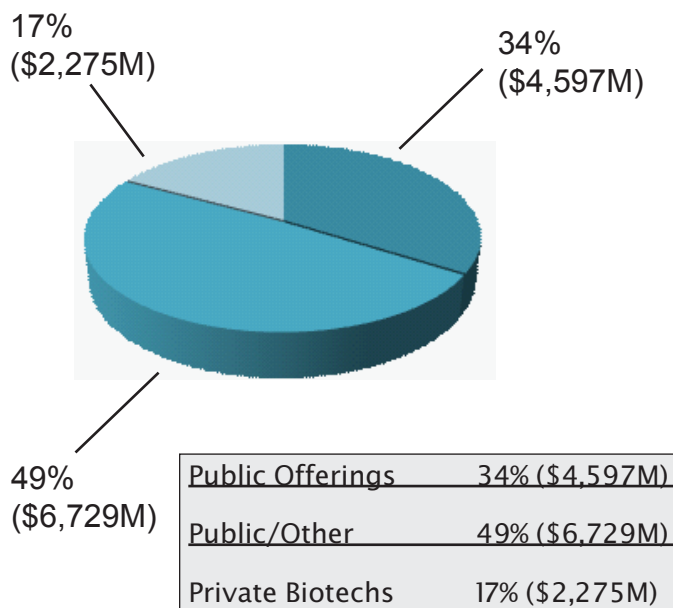
Although the FDA is not bound to follow ODAC's advice, analysts expect the agency to grant Adcetris (brentuximab vedotin) its two accelerated approvals. And while the move may not warrant read-through to anyone else in the queue, it is perhaps at least a sign that the accelerated approval pathway can still live up to its mantra and help speed important new drugs to patients who need them, as long as drugmakers can still be incentivized to give it a try. ■

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## Money Raised By Biotech: Jan. 1 - Jul. 15, 2011



eventually create licenses for specific technologies. “We can read the real signal and wash the distracters away,” said Barbara Handelin, president of BioPontis.

But just licensing good compounds isn’t enough. “You have to find a way to incorporate experience and interest in your ultimate customer up front,” Handelin said. So the firm signed up three large pharma players: Merck & Co. Inc., Pfizer Inc. and Janssen Biotech Inc., a subsidiary of Johnson & Johnson. As part of the alliance, BioPontis will be informed on a confidential level of their interest in particular disease areas or even specific targets. More importantly, the potential licensors also will contribute their knowledge, which will help BioPontis meet pharma’s requirements to license the drugs.

BioPontis is setting up a \$50 million fund that will come from investment firms looking for returns, but also is expected to contain contributions from strategic LPs, small and mid-cap product companies and CROs that will have options to acquire molecules that BioPontis is developing.

The fund is expected to support 20 to 25 projects, but that assumes a failure rate of 75 percent, said Richard Basile, BioPontis’ CEO. He hopes the first fund can serve as a pilot project that can propel the firm to bring in more academic institutions and pharma partners.

## Corporations

*Continued from page 1*

Burch, vice president of Calvert Research.

The firm typically assigns between 30 percent and 50 percent of the cost of CRO services toward an equity stake in a company. The financing bridge is intended to get the molecule to investigational new drug application in two years or less, at which time a larger player can take over.

For example, Calvert Research invested in CureDM LLC to help develop its diabetes treatment, Pancreate, which is designed to stimulate the body’s production of insulin-producing islet cells. Last year, Sanofi SA licensed rights to Pancreate for a potential \$335 million in up-front and milestone payments. Even though the deal was back-end loaded, Burch said “it was profitable for us and the other shareholders” with just the up-front payments. (See *BioWorld Today*, April 9, 2010.)

While the CRO investment model can be successful, it’s partially limited by the control that the investment arms have in the development of the drug. “Since we are minority investors, we try to be very careful about who we’re doing business with and how we’re doing the business,” Burch said.

## Improving the Signal to Noise

BioPontis Alliance LLC is attempting to bridge the funding gap by setting up alliances on both sides of the valley of death. Over the last two years, the firm has established agreements with eight academic institutions as well as several big pharmas.

The academic agreements allow BioPontis to sort through the myriad of technology coming out of the institutions and

## Venture 2.0

Atlas Venture is using some of the money from its eighth venture capital fund to develop drugs through newly formed Atlas Venture Development Corp. The group has evaluated 200 compounds and has closed two deals that have yet to be disclosed publicly.

Working out of the same offices as the venture firm, AVDC will develop drugs virtually through proof of concept to de-risk the asset and increase its value. In some cases, AVDC may bring in syndicate partners to co-invest in the development of licensed assets.

In its previous fund, the firm backed multiple single-asset companies that developed their compounds virtually. “AVDC is an extension and institutionalization of that concept,” said Booth.

Unlike typical venture-backed companies, AVDC strives to have a defined path of liquidity in place when it licenses molecules. Drug companies that out-license assets will have the option to reacquire the asset at predefined terms in much the same manner that Flexion Therapeutics, the product development firm run by management that developed Eli Lilly and Co.’s Chorus division, has used. And for compounds brought in from academic institutions, AVDC will line up potential buyers for drugs before they’re even hovering over the valley of death. (See *BioWorld Today*, Feb. 1, 2010.)

Venture firm CMEA Capital has set up a similar company, Velocity Pharmaceutical Development, which will consolidate multiple virtually developed drugs under a single umbrella. Like AVDC and BioPontis, the team at Velocity has spent a considerable amount of time figuring out exactly what

*See Corporations, page 5*

## WEEK IN REVIEW

**Financings**

**Horizon Pharma Inc.** set terms for its proposed initial public offering (IPO), which would gross \$60.5 million at the midpoint.

**Insite Vision Inc.** is raising \$22.2 million in a private placement of stock and warrants.

**Merrimack Pharmaceuticals Inc.** filed to raise up to \$172.5 million in an IPO.

**Prana Biotechnology Ltd.** set up an at-the-market offering worth about \$10 million at current prices.

**Tarsa Therapeutics Inc.** raised \$24.5 million in venture financing through an internal round.

**Verastem Inc.** raised \$32 million in a Series B financing.

**Deals**

**Array BioPharma Inc.** licensed ARRY-543 to **Aslan Pharmaceuticals Pte Ltd.** for Phase II trials.

**Micromet Inc.** got \$14 million up front in a potential \$976 million antibody discovery deal with **Amgen Inc.**

**Onconova Therapeutics Inc.** licensed rigosertib rights in Japan and Korea to **SymBio Pharmaceuticals Ltd.**

**Zogenix Inc.** teamed up with **Durect Corp.** in a \$105 million deal for long-acting risperidone.

**... And More**

**Amylin Pharmaceuticals Inc., Eli Lilly and Co.** and **Alkermes Inc.**'s Bydureon (exenatide extended-release) met its endpoints in a confirmatory thorough QT study.

**Halozyyme Therapeutics Inc.** and **Baxter International Inc.** got good Phase III data with HyQ immune globulin.

**Human Genome Sciences Inc.** and **GlaxoSmithKline plc** won European approval of lupus drug Benlysta (belimumab).

**Sanofi SA**'s multiple sclerosis drug Lemtrada (alemtuzumab) hit its Phase III endpoint, but faces fierce competition.

**Seattle Genetics Inc.**'s Adcetris (brentuximab vedotin) got unanimous support from ODAC for accelerated approval in two lymphoma indications.

**Titan Pharmaceuticals Inc.**'s Probuphine (subcutaneous buprenorphine) got good Phase III data in opioid addiction.

**Transcept Pharmaceuticals Inc.** said it doesn't expect approval for insomnia drug Intermezzo (sublingual zolpidem).

**Corporations**

*Continued from page 4*

pharma wants in proof-of-concept studies to make licensing easier. (See *BioWorld Insight*, July 5, 2010.)

**Sharing the Risk**

For academic and biopharma firms with drugs they don't want to develop, the beauty of product development companies is the ability to hand off the development risk, albeit by sacrificing much of the upside potential.

Start-up GlycoRegImmune Inc. took advantage of the risk transfer when it brought in RxMD Inc. to develop the portfolio of drug candidates arising from its natural killer T cell targeted technology. RxMD is an 11-year old consulting firm that recently decided to use the cash generated from its fee-for-services business to fund product development. "We're funding the risk," said Sanjay Shukla, CEO of RxMD. Instead of taking a consulting fee, RxMD is willing to accept equity in the product, commercial rights in India, milestone payments or a combination thereof.

The RxMD deal with GlycoRegImmune was just announced this month, and BioPontis' deals with Pfizer and Janssen were unveiled just a few weeks before, as was CMEA's launch of Velocity. Other recent deals – like Array BioPharma Inc.'s decision last week to outlicense Phase II development of

ARRY-543 to Singapore-based Aslan Pharmaceuticals Pte Ltd. – also seem to indicate that the product development company business model is gaining traction.

There are certainly benefits, even beyond capital efficiency. Depending on the system employed, inventors can retain some control over development despite losing the upside potential. In BioPontis' model for instance, academics have a seat at the development table. Handelin sounded downright giddy about the "novel experience" that academics might have in designing the "killer experiments" to bridge the gaps required to get drugs in the hands of pharma.

Also, because the risk is in the hands of the development company, the decision on whether to continue development of a drug ultimately rests in their hands as well – hands that tend to be less biased by attachment to projects. By killing projects early, companies can keep costs down, which is especially important for development companies that have capped their upside by agreeing to acquisition terms with a pharma ahead of time.

For now, the biggest unknown with product development company models is how their assumption of risk will be rewarded, and whether that reward will be sufficient to drive further uptake of certain models. Despite that uncertainty, "there is clearly a lot of experimentation, and I think you will see more interesting deals," said Alexis Borisy, partner with Third Rock Ventures. ■

## WORD ON THE STREET

“It disturbs me that people are willing to accept this: treating the symptoms and allowing the disease to progress.”  
– Jerry Colca, president and chief scientific officer at Metabolic Solutions Development Co., on new diabetes drugs

“It’s easy to waste other people’s money . . . Price becomes no object.”  
– Avik Roy, Monnes, Crespi, Hardt & Co. analyst, testifying at the House Subcommittee hearing on the Independent Payment Advisory Board

“No one should have to go through all the pain and suffering that I did when I was on chemotherapy.”  
– Logan Emmons, a teenager with anaplastic large-cell lymphoma, testifying at the Oncologic Drugs Advisory Committee meeting for Seattle Genetics Inc.’s Adcetris (brentuximab vedotin)

## WEEK IN WASHINGTON

The FDA’s Janet Woodcock gave a sneak peak at PDUFA V enhancements, which include more meetings with sponsors, an expanded ability to use biomarkers, standardized REMS and more.

Several biopharma firms filed a citizen petition asking the FDA to clarify off-label promotion policies.

### PPAR

*Continued from page 2*

the FDA restricting the use of Actos, but he blames many of the problems of both drugs on their mechanism of action as PPAR-gamma agonists.

Pharma’s mistake was believing the thiazolidinediones derived their efficacy from targeting PPAR-gamma, explained Colca, who worked on the early development of Actos. Instead, the efficacy comes from a mitochondrial target that affects the metabolic inflammation underlying insulin resistance, and PPAR-gamma contributes little beyond unwanted side effects.

That’s why Avandia – a powerful PPAR-gamma agonist – had such trouble with cardiovascular side effects, while Actos – which doesn’t bind PPAR-gamma as strongly – did not, Colca said. He added that PPAR-gamma agonism is also likely responsible for Actos’ increased weight gain and decreased hematocrit effects, although he said the bladder cancer issue is probably not a class effect and he is not yet convinced it is a real effect at all.

Even the next-generation, selectively acting PPAR-gamma agonists – like those in development by InteKrin Therapeutics Inc., Metabolex Inc. and others – are likely to face the same problems, he said.

“We recognized that all of pharma had gone in the wrong direction,” Colca said. That’s why he founded Kalamazoo, Mich.-based MSDC, which recently completed Phase IIa trials with MSDC-0160, an isomer of a pioglitazone metabolite. The data showed MSDC-0160 lowered glucose levels, increased insulin sensitivity, lowered blood pressure and increased HDL levels, all without the weight gain and

hematocrit effects of Actos.

A 350-patient Phase IIb trial is underway, with data expected around the end of the year. MSDC is also conducting a Phase IIa trial with MSDC-0602, an analog specifically engineered to avoid PPAR-gamma. Data are expected in August.

Getting the word out on MSDC’s research to potential partners has been challenging, Colca said, since big pharma has been burned so many times before in the diabetes space. But the potential to not just treat, but prevent diabetes is hard to ignore – particularly if it can be done without the side effects of existing treatments.

“I think people are staring to get the message,” Colca said. ■

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## Top 10 Deals Between Biotech Companies: 2011

| Company                                | Company                     | Deal Value        |
|----------------------------------------|-----------------------------|-------------------|
| Vertex Pharmaceuticals Inc.            | Alios Biopharma Inc.        | \$1.5B (June)     |
| Amgen Inc.                             | Micromet Inc.               | \$976M (July)     |
| Xencor Inc.                            | Amgen Inc.                  | \$500M (January)  |
| Human Genome Sciences Inc.             | FivePrime Therapeutics Inc. | \$495M (March)    |
| Molecular Partners AG                  | Allergan Inc.               | \$420M (May)      |
| Progenics Inc.                         | Salix Inc.                  | \$350M (February) |
| Valeant Pharmaceuticals Internat. Inc. | Meda AB                     | \$326M (July)     |
| Merrimack Pharmaceuticals Inc.         | PharmaEngine Inc.           | \$220M (May)      |
| Medicis                                | Anacor Pharmaceuticals Inc. | \$160M (February) |
| MAP Pharmaceuticals Inc.               | Allergan Inc.               | \$157M (February) |

## Biotechnology Company Deals With Other Biotechnology Companies: June 1 - July 15, 2011

**TOTAL VALUE IN 2011: \$6,224.72M\***

NUMBER OF DEALS IN 2011: 125

| Company (Location)                                           | Company (Location)                                            | Value (M) | Type/Product Area                                                                                                                                                                   | Terms/Details (Date)                                                                                                                                   |
|--------------------------------------------------------------|---------------------------------------------------------------|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>JUNE</b>                                                  |                                                               |           |                                                                                                                                                                                     |                                                                                                                                                        |
| <b>Advanced Cell Technology Inc.</b><br>(Marlborough, Mass.) | <b>Roslin Cells Ltd.</b><br>(Midlothian, Scotland)            | ND        | Collaboration to establish a bank of GMP-grade human embryonic stem cell lines                                                                                                      | They will use ACT's single-cell blastomere technique for deriving hESC lines without destroying embryos (6/22)                                         |
| <b>Agenus Inc.</b><br>(Lexington, Mass.)                     | <b>Integrated BioTherapeutics Inc.</b><br>(Gaithersburg, Md.) | ND        | License agreement for the use of Antigenics' SQ-21 Stimulon adjuvant in the development of a vaccine against Ebola and Marburg viruses                                              | Agenus said it is entitled to receive a license fee and potential milestone payments and worldwide royalties on net sales (6/15)                       |
| <b>EntreMed Inc.</b><br>(Rockville, Md.)                     | <b>Selected Value Therapeutics I LLC</b>                      | ND        | Selected Value exercised its right to acquire an exclusive license to develop and commercialize the Phase II oncology candidate, ENMD-2076, in China and certain of its territories | EntreMed is entitled to certain development milestone payments, as well as royalties on future product sales (6/8)                                     |
| <b>Flamel Technologies SA</b> (Lyon, France)                 | <b>Digna Biotech SL</b><br>(Madrid, Spain)                    | ND        | Joint development agreement for the preclinical and clinical development of PI44, PI7 and Methylthiadenosine (MTA)                                                                  | Flamel is responsible for formulation and manufacturing process development, and Digna is responsible for pre-clinical and clinical development (6/28) |

| Company (Location)                                         | Company (Location)                                                 | Value (M) | Type/Product Area                                                                                                                                 | Terms/Details (Date)                                                                                                                                                                                                                                                 |
|------------------------------------------------------------|--------------------------------------------------------------------|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Forma Therapeutics Inc.</b> (Cambridge, Mass.)          | <b>Genentech Inc.</b> (subsidiary of Roche AG; Basel, Switzerland) | ND        | Exclusive worldwide rights agreement to acquire a pre-clinical small-molecule program against a single undisclosed cancer target                  | Forma gets an undisclosed up-front payment, research funding and potential milestone payments; Genentech has the option to acquire the compound for an undisclosed buyout payment and additional commercial milestone payments (6/28)                                |
| <b>Generex Biotechnology Corp.</b> (Worcester, Mass.)      | <b>Amarantus BioScience Inc.</b> (Sunnyvale, Calif.)               | \$10      | Licensing agreement for RapidMist buccal drug delivery technology                                                                                 | Amarantus will pay a \$10M license fee to use RapidMist in the development of its MANF proteins for Parkinson's disease and diabetes mellitus (6/1)                                                                                                                  |
| <b>GlycoRegImmune Inc.</b> (San Diego)                     | <b>RxMD Inc.</b> (San Diego)                                       | ND        | Collaboration to develop drugs for inflammatory, autoimmune and neurodegenerative conditions                                                      | GlycoRegimmune has technologies targeting natural killer T cells (6/30)                                                                                                                                                                                              |
| <b>Grifols S.A.</b> (Barcelona, Spain)                     | <b>Kedrion S.p.A.</b> (Castelvecchio Pascoli, Italy)               | ND        | Sale of U.S. facilities that will give Kedrion its first entry into the U.S. plasma-derived drug market                                           | The sale is part of a settlement of a Federal Trade Commission complaint about Grifols' \$3.4B acquisition of Talecris Biotherapeutics Holdings Corp.; Grifols will manufacture globulin, albumin and plasma-derived Factor VIII for Kedrion for several years (6/6) |
| <b>Halozyme Therapeutics Inc.</b> (San Diego)              | <b>Intrexon Corp.</b> (Research Triangle Park, N.C.)               | \$63      | Collaboration on Intrexon's recombinant human alpha 1-antitrypsin (AIAT) developed using Halozyme's subcutaneous Enhance platform                 | The deal includes \$9M up front, with the remaining \$54M coming in milestones, plus up to an 11% royalty rate on future sales of AIAT (6/8)                                                                                                                         |
| <b>iCo Therapeutics Inc.</b> (Vancouver, British Columbia) | <b>Immune Pharmaceuticals</b> (Tel Aviv, Israel)                   | \$33.7    | Licensing agreement for bertilimumab for systemic uses                                                                                            | iCo will receive \$500,000 up front, plus 600,000 Immune shares, worth about \$1.2M, plus \$32M in milestones and royalties (6/27)                                                                                                                                   |
| <b>ImmunoCellular Therapeutics Ltd.</b> (Los Angeles)      | <b>BioWa Inc.</b> (Princeton, N.J.)                                | ND        | Deal to gain access to BioWa's Potelligent technology platform for use in developing antibody-dependent cellular cytotoxicity-enhanced antibodies | BioWa will receive the right to certain antibody technology from ImmunoCellular in exchange, as well as selected option rights to ImmunoCellular's antibodies using the Potelligent platform (6/3)                                                                   |

| Company (Location)                                             | Company (Location)                                | Value (M) | Type/Product Area                                                                                                           | Terms/Details (Date)                                                                                                                                                                                                                                                                               |
|----------------------------------------------------------------|---------------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>IntelGenx Corp.</b> (Saint Laurent, Quebec)                 | <b>RedHill Biopharma Ltd.</b> (Tel Aviv, Israel)  | \$2.3     | Agreement to co-develop and license an antipsychotic oral thin film product based on its VersaFilm drug delivery technology | RedHill would obtain exclusive worldwide rights to market and sell IntelGenx's product in exchange for upfront, milestone and external development fees totaling up to \$2.3M; upon commercialization, IntelGenx would receive up to 50% of all proceeds (6/15)                                    |
| <b>Kareus Therapeutics SA</b> (La Chaux-de-Fonds, Switzerland) | <b>Quintiles</b> (Research Triangle Park, N.C.)   | ND        | Deal to develop two preclinical programs                                                                                    | Quintiles will make a seven-figure investment divided between equity and clinical services on a shared-risk basis; Quintiles will carry out Phase I proof-of-relevance trials on Kareus's Alzheimer's candidate, KU-046, and an unselected Type II diabetes candidate (6/14)                       |
| <b>Ligand Pharmaceuticals Inc.</b> (San Diego)                 | <b>The Medicines Co.</b> (Parsippany, N.J.)       | \$23.75   | Licensing agreement for worldwide rights to a Captisol-enabled intravenous formulation of Plavix                            | Ligand will receive \$1.75M up front and as much as \$22M in milestone payments, plus double-digit royalties on sales (6/6)                                                                                                                                                                        |
| <b>Pluristem Ltd.</b> (Haifa, Israel)                          | United Therapeutics (Silver Spring, Md.)          | \$62      | A \$62M partnership for Pluristem's PLacental eXpanded (PLX) cell pipeline                                                  | Pluristem will get \$7M up front with \$55M in milestone and other payments, and United Therapeutics gets exclusive worldwide licensing rights to develop and commercialize a PLX cell-based treatment for pulmonary hypertension; Pluristem also is entitled to royalties on gross profits (6/21) |
| <b>Vertex Pharmaceuticals Inc.</b> (Cambridge, Mass.)          | <b>Alios BioPharma Inc.</b> (South San Francisco) | \$1.525B  | Deal for worldwide rights to preclinical nucleotide analogues ALS-2200 and ALS-2158                                         | Vertex will pay Alios \$60M up front, potential R&D milestones of as much as \$715M, with about \$35M expected to be paid in 2011, as much as \$750M in sales milestones, and tiered royalties on product sales (6/14)                                                                             |
| <b>JULY</b>                                                    |                                                   |           |                                                                                                                             |                                                                                                                                                                                                                                                                                                    |
| <b>Acorda Therapeutics Inc.</b> (Hawthorne, N.Y.)              | <b>Medtronic Inc.</b> (Minneapolis)               | \$35      | Worldwide development and commercialization rights agreement for ACI05                                                      | The deal is worth \$35M, including \$3M up front, \$32M in regulatory and milestone payments, and single-digit royalties (7/6)                                                                                                                                                                     |

| Company (Location)                               | Company (Location)                         | Value (M) | Type/Product Area                                                                                                                                               | Terms/Details (Date)                                                                                                                                                                                                                           |
|--------------------------------------------------|--------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Amgen Inc.</b> (Thousand Oaks, Calif.)        | <b>Micromet Inc.</b> (Rockville, Md.)      | \$976     | Agreement for Micromet to provide discovery and pre-clinical development of BiTE antibodies against three solid tumor targets                                   | Amgen will take over costs for development and commercialization of antibodies advanced to the investigational new drug application stage; the \$976M value includes \$14M up front, plus milestones, royalties and development funding (7/12) |
| <b>Bluebird Bio</b> (Cambridge, Mass.)           | <b>GenOway SA</b> (Lyon, France)           | ND        | Exclusive license agreement for RMCE technology for making knock-in rodents for laboratory use                                                                  | Terms were not disclosed (7/13)                                                                                                                                                                                                                |
| <b>Durect Corp.</b> (Cupertino, Calif.)          | <b>Zogenix Inc.</b> (San Diego)            | ND        | Licensing agreement for clinical development and commercialization of a long-acting, injectable formulation of risperidone using technology developed by Durect | Zogenix expects to begin clinical studies of the resulting product candidate, Relday, in patients with schizophrenia in early 2012 (7/13)                                                                                                      |
| <b>Evotec AG</b> (Hamburg, Germany)              | <b>UCB SA</b> (Brussels, Belgium)          | ND        | Three-year collaboration to identify small-molecule modulators of biological targets selected by UCB in the area of central nervous system disorders            | Evotec will receive a fixed research funding fee over the term of the collaboration and is eligible for milestones, plus royalties (7/11)                                                                                                      |
| <b>Onconova Therapeutics Inc.</b> (Newtown, Pa.) | <b>SymBio Pharmaceuticals Ltd.</b> (Tokyo) | ND        | Development and commercialization rights agreement for Japan and Korea for rigosertib                                                                           | Onconova will receive an undisclosed up-front payment, development and sales milestones, plus royalties (7/11)                                                                                                                                 |

## Notes:

The date indicated refers to the *BioWorld Today* issue in which the news item can be found.

\* The total value represents the amount of disclosed money involving collaborations between biotechnology companies, including manufacturing, marketing and distribution agreements detailed in the following chart.

\*\* Denotes the date the item ran in *BioWorld International*.

## Manufacturing, Marketing And Distribution Agreements Between Biotech Companies: June 1 - July 15, 2011

| Company (Location)                                                       | Company (Location)                                                     | Value (M) | Type/Product Area                                                                                          | Terms/Details (Date)                                                                                                                                                                                                                                                                                     |
|--------------------------------------------------------------------------|------------------------------------------------------------------------|-----------|------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>JUNE</b>                                                              |                                                                        |           |                                                                                                            |                                                                                                                                                                                                                                                                                                          |
| <b>Somaxon Pharmaceutical Inc.</b><br>(San Diego)                        | <b>Paladin Labs Inc.</b><br>(Montreal)                                 | \$134     | Agreement to commercialize Silenor to treat insomnia in Canada, South America and Africa                   | Paladin will pay Somaxon \$500,000 up front, buy 2.18M shares of Somaxon common stock for \$5M, and provide a potential \$128.5M in milestone payments (6/9)                                                                                                                                             |
| <b>JULY</b>                                                              |                                                                        |           |                                                                                                            |                                                                                                                                                                                                                                                                                                          |
| <b>Valeant Pharmaceuticals International Inc.</b><br>(Mississauga, Ont.) | <b>Meda AB</b> (Solna, Sweden)                                         | \$326     | Agreement to acquire North American rights to Elidel and Xerese from Meda                                  | Valeant will pay \$76M up front and milestones and royalties totaling about \$130M, plus a double-digit royalty on net sales of Elidel, Xerese and Zovirax that includes additional minimum royalties of \$120M during 2013-2015; Valeant holds exclusive rights to Zovirax in the U.S. and Canada (7/5) |
| <b>Vanda Pharmaceuticals Inc.</b><br>(Rockville, Md.)                    | <b>Probiomed SA de CV</b><br>(unit of Proquifin SA de CV; Mexico City) | ND        | Exclusive license agreement for the commercialization of schizophrenia drug Fanapt (iloperidone) in Mexico | Financial terms were not disclosed (7/12)                                                                                                                                                                                                                                                                |

## Notes:

The date indicated refers to the *BioWorld Today* issue in which the news item can be found.

\*\* Denotes the date the item ran in *BioWorld International*.

## Biotech–Biotech Collaborations: Modified Agreements: June 1 - July 15, 2011

| Company (Location)                                                                                                                                                                 | Company (Location)                                                                        | Value (M) | Type/Product Area                                                                                                                             | Terms/Details (Date)                                                                                                                                                                                                                                                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>I. MODIFIED AGREEMENTS</b>                                                                                                                                                      |                                                                                           |           |                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                       |
| <b>JUNE</b>                                                                                                                                                                        |                                                                                           |           |                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                       |
| <b>Medivir AB</b> (Huddinge, Sweden)                                                                                                                                               | <b>Meda AB</b> (Solna, Sweden)                                                            | \$45      | Revised commercial agreement covering the U.S., Canada and Mexico for the cold sore product Xerese and agreed to terms on a second indication | Medivir decided to forgo a future revenue stream from North American sales in return for a \$45M payment from Meda, which now gains exclusive rights for genital herpes; Medivir would receive a \$10M milestone payment should Xerese gain approval in this indication; it also could receive single-digit royalties on sales (6/30) |
| <b>Seattle Genetics</b> (Bothell, Wash.)                                                                                                                                           | <b>Agensys Inc.</b> (Santa Monica, Calif.; affiliate of Tokyo-based Astellas Pharma Inc.) | ND        | Exercised option to co-develop a second antibody-drug conjugate under their collaboration agreement                                           | The ADC, known as ASG-22ME, targets the Nectin-4 antigen, which is expressed on multiple solid tumors (6/10)                                                                                                                                                                                                                          |
| <b>I. TERMINATED AGREEMENTS</b>                                                                                                                                                    |                                                                                           |           |                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                       |
| <b>RESprotect GmbH</b> (Dresden, Germany)                                                                                                                                          | <b>SciClone Pharmaceuticals Inc.</b> (Foster City, Calif.)                                | ND        | RESprotect received back North American rights for anticancer drug RPI01                                                                      | SciClone discontinued a Phase II trial in 2009, and RESprotect intends to reinitiate development this year (6/29)                                                                                                                                                                                                                     |
| Notes:<br>The date indicated refers to the <i>BioWorld Today</i> issue in which the news item can be found.<br>** Denotes the date the item ran in <i>BioWorld International</i> . |                                                                                           |           |                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                       |

## The Week's Biggest Gainers and Losers

### 10 BIGGEST U.S. WINNERS FOR THE WEEK

| (By Percent)     |       | (By Dollars)       |      |
|------------------|-------|--------------------|------|
| Rosetta Genomics | 32.76 | Alexion Pharma     | 2.07 |
| Cortex Pharma    | 25.00 | ImmunoGen 1.25     |      |
| Unigene 18.81    |       | Infinity Pharma    | 1.11 |
| Access Pharma    | 17.82 | United Therap      | 0.89 |
| Tengion 14.66    |       | Alnylam Pharma     | 0.82 |
| Infinity Pharma  | 13.79 | BioMarin Pharma    | 0.81 |
| Idenix Pharma    | 12.59 | Idenix Pharma      | 0.68 |
| Zogenix 12.53    |       | Targacept          | 0.60 |
| Discovery Labs   | 11.16 | Pharmacyclics 0.59 |      |
| Titan Pharma     | 10.80 | Spectrum Pharma    | 0.58 |

### 10 BIGGEST U.S. LOSERS FOR THE WEEK

| (By Percent)       |        | (By Dollars)     |       |
|--------------------|--------|------------------|-------|
| Transcept Pharma   | -38.97 | Regeneron Pharma | -4.05 |
| Generex Biotech    | -36.36 | Biogen Idec      | -3.39 |
| Alseres -33.33     |        | Transcept Pharma | -3.11 |
| StemCells -25.82   |        | Acorda Thera     | -2.82 |
| Labopharm -20.00   |        | Amgen            | -2.59 |
| Oxis International | -20.00 | Endocyte         | -2.58 |
| Endocyte -17.68    |        | Pharmasset -2.37 |       |
| Somaxon Pharma     | -13.51 | Seattle Genetics | -2.21 |
| MDRNA -13.04       |        | Sagent Pharma    | -1.96 |
| Seattle Genetics   | -10.48 | Onyx Pharma      | -1.92 |

## BioWorld Stock Report For Public Biotechnology Companies

| Company            | Symbol | Close 7/8 | Close 7/15 | %Change WK | %Change YTD | Vol (000) |
|--------------------|--------|-----------|------------|------------|-------------|-----------|
| 3S Bio             | SSRX   | 18.57     | 17.96      | -3.28      | 19.89       | 388       |
| Aastrom Biosci     | ASTM   | 2.73      | 2.65       | -2.93      | 3.52        | 1356      |
| Acadia Pharma      | ACAD   | 1.83      | 1.7        | -7.10      | 38.21       | 848       |
| Accentia Biopharma | ABPI   | 0.46      | 0.45       | -2.17      | -40.00      | 265       |
| Access Pharma      | ACCP   | 1.74      | 2.05       | 17.82      | -16.33      | 168       |
| AcelRx Pharma      | ACRX   | 4.25      | 4.42       | 4.00       | -2.86       | 35        |
| Achillion ACHN     |        | 8.08      | 7.49       | -7.30      | 84.48       | 4319      |
| Acorda Therap      | ACOR   | 32.45     | 29.63      | -8.69      | 7.71        | 2739      |
| Adamis ADMP        |        | 0.22      | 0.22       | 0.00       | 7.32        | 226       |
| Adolor ADLR        |        | 2.63      | 2.43       | -7.60      | 95.97       | 2684      |
| Aegerion Pharma    | AEGR   | 15.76     | 15.22      | -3.43      | 7.41        | 196       |
| AEterna Zentaris   | AEZS   | 2.31      | 2.31       | 0.00       | 32.00       | 7769      |
| Affymax AFFY       |        | 7.11      | 7.43       | 4.50       | 11.73       | 3179      |
| Agenus AGEN        |        | 0.82      | 0.77       | -6.10      | -23.76      | 1002      |
| Albany Molecular   | AMRI   | 4.98      | 4.84       | -2.81      | -17.69      | 349       |
| Alexion Pharma     | ALXN   | 50.3      | 52.37      | 4.12       | -35.07      | 8629      |
| Alexza Pharma      | ALXA   | 1.81      | 1.7        | -6.08      | 34.92       | 2116      |
| Alimera Sciences   | ALIM   | 8.58      | 8.76       | 2.10       | -14.20      | 435       |
| Alkermes ALKS      |        | 19.52     | 19.27      | -1.28      | 56.67       | 4802      |
| Allos Therapeutics | ALTH   | 2.14      | 2          | -6.54      | -56.71      | 2903      |
| Alnylam Pharma     | ALNY   | 9.44      | 10.26      | 8.69       | 3.85        | 1052      |
| Alseres ALSE       |        | 0.15      | 0.1        | -33.33     | -23.08      | 72        |
| AMAG Pharma        | AMAG   | 19.3      | 18.27      | -5.34      | 0.55        | 1041      |
| Amarin AMRN        |        | 14.81     | 13.63      | -7.97      | 64.41       | 7911      |
| Amgen AMGN         |        | 57.64     | 55.05      | -4.49      | -0.86       | 29024     |
| Amicus FOLD        |        | 7.33      | 7.5        | 2.32       | 56.58       | 363       |
| Ampliphi Biosci    | APHB   | 0.23      | 0.24       | 4.35       | -4.00       | 299       |
| Amylin Pharma      | AMLN   | 14.22     | 12.83      | -9.77      | -13.83      | 10622     |
| Anacor Pharma      | ANAC   | 6.78      | 6.46       | -4.72      | 20.30       | 124       |
| Anthera Pharma     | ANTH   | 8.08      | 8.01       | -0.87      | 64.48       | 297       |
| Ardea Biosciences  | RDEA   | 25.88     | 24.73      | -4.44      | -5.90       | 465       |
| Arena Pharma       | ARNA   | 1.51      | 1.44       | -4.64      | -15.79      | 6971      |
| Ariad Pharma       | ARIA   | 12.16     | 12.58      | 3.45       | 142.86      | 15318     |
| ArQule ARQL        |        | 6.49      | 6.33       | -2.47      | 9.33        | 718       |
| Array BioPharma    | ARRY   | 2.58      | 2.5        | -3.10      | -16.11      | 1292      |
| Aryx AR            | YX     | 0.03      | 0.03       | 0.00       | -88.89      | 431       |
| Auxilium Pharma    | AUXL   | 20.36     | 20.37      | 0.05       | -3.96       | 3134      |
| Avanir A           | VNR    | 3.53      | 3.39       | -3.97      | -15.46      | 5060      |
| Avax Tech          | AVXT   | 0.03      | 0.03       | 0.00       | -33.33      | 99        |
| AVEO Pharma        | AVEO   | 20.68     | 20.03      | -3.14      | 36.26       | 2066      |
| AVI BioPharma      | AVII   | 1.65      | 1.61       | -2.42      | -25.46      | 3525      |
| Bellus Health      | BLUS   | 0.06      | 0.06       | 0.00       | -61.29      | 48        |
| BG Medicine        | BGMD   | 8.29      | 8.33       | 0.48       | 0.36        | 62        |
| BioCryst Pharma    | BCRX   | 3.92      | 3.93       | 0.26       | -23.39      | 587       |
| Biodel BIOD        |        | 1.98      | 2.01       | 1.52       | 4.69        | 1175      |
| Biodelivery Sci    | BDSI   | 3.54      | 3.62       | 2.26       | -2.16       | 551       |
| Biogen Idec        | BIIB   | 107.39    | 104        | -3.16      | 55.69       | 7261      |
| BioMarin Pharma    | BMRN   | 28.88     | 29.69      | 2.80       | 9.27        | 7160      |
| Bio-path Holdings  | BPTH   | 0.31      | 0.3        | -3.23      | -16.67      | 83        |
| BioSante Pharma    | BPAX   | 3.6       | 3.64       | 1.11       | 119.28      | 24246     |
| Cadence Pharma     | CADX   | 9.06      | 8.62       | -4.86      | 14.32       | 1222      |
| Cardiome CRME      |        | 4.45      | 4.23       | -4.94      | -35.42      | 651       |
| Cardiovascular Bio | CVBT   | 0.32      | 0.32       | 0.00       | -5.88       | 399       |
| Catalyst Pharma    | CPRX   | 1.75      | 1.5        | -14.29     | 56.25       | 413       |
| Celgene CELG       |        | 61.99     | 60.67      | -2.13      | 2.09        | 9153      |

| Company            | Symbol | Close 7/8 | Close 7/15 | %Change WK | %Change YTD | Vol (000) |
|--------------------|--------|-----------|------------|------------|-------------|-----------|
| Cell Therapeutics  | CTIC   | 1.48      | 1.39       | -6.08      | 273.66      | 6676      |
| Celldex Therap     | CLDX   | 3.69      | 3.71       | 0.54       | -11.03      | 1179      |
| CEL-SCI CVM        |        | 0.5       | 0.5        | 0.00       | -39.93      | 1138      |
| Cephalon CEPH      |        | 80.18     | 79.99      | -0.24      | 28.68       | 13536     |
| Cerus CERS         |        | 2.92      | 2.86       | -2.05      | 15.32       | 957       |
| Chelsea Therap     | CHTP   | 5.81      | 5.89       | 1.38       | -22.40      | 2967      |
| Cleveland Biolabs  | CBLI   | 3.32      | 3.13       | -5.72      | -56.47      | 1223      |
| Codexis CDXS       |        | 9.98      | 9.26       | -7.21      | -12.64      | 460       |
| Columbia Labs      | CBRX   | 3.39      | 3.19       | -5.90      | 45.66       | 2690      |
| CombiMatrix        | CBMX   | 3.43      | 3.33       | -2.92      | 49.33       | 32        |
| Complete Genomics  | GNOM   | 14.76     | 14.7       | -0.41      | 96.79       | 1018      |
| Compugen           | CGEN   | 4.27      | 4.02       | -5.85      | -19.28      | 210       |
| Corcept COR        | T      | 3.89      | 3.81       | -2.06      | -2.81       | 729       |
| CorMedix CRMD      |        | 1.49      | 1.45       | -2.68      | -17.61      | 2         |
| Cornerstone Therap | CRTX   | 9.14      | 8.6        | -5.91      | 52.21       | 141       |
| Cortix Pharma      | CORX   | 0.08      | 0.1        | 25.00      | -44.44      | 313       |
| Cubist Pharma      | CBST   | 36.6      | 35.9       | -1.91      | 66.36       | 5979      |
| Curis CRIS         |        | 3.99      | 3.99       | 0.00       | 97.52       | 1908      |
| Cytokinetics CYTK  |        | 1.21      | 1.3        | 7.44       | -37.80      | 2494      |
| CytRx CYTR         |        | 0.78      | 0.73       | -6.41      | -27.00      | 1487      |
| Dara Biosciences   | DARA   | 2.46      | 2.55       | 3.66       | -24.33      | 117       |
| Dendreon DNDN      |        | 40.67     | 38.8       | -4.60      | 9.57        | 9757      |
| DepoMed DEPO       |        | 8.74      | 8.31       | -4.92      | 28.24       | 3415      |
| DiaDexus DDXS      |        | 0.34      | 0.32       | -5.88      | 10.34       | 36        |
| Discovery Labs     | DSCO   | 2.33      | 2.59       | 11.16      | -22.22      | 2621      |
| DURECT DRRX        |        | 2.03      | 2.11       | 3.94       | -40.56      | 2119      |
| Dusa Pharma        | DUSA   | 5.91      | 5.54       | -6.26      | 125.20      | 1056      |
| Dyax DY            | AX     | 2.06      | 2.03       | -1.46      | -2.87       | 2235      |
| Dynavax DV         | AX     | 2.89      | 3.02       | 4.50       | -2.58       | 9225      |
| Emergent BioSol    | EBS    | 21.78     | 21.76      | -0.09      | -8.11       | 1099      |
| Emisphere Tech     | EMIS   | 0.9       | 0.92       | 2.22       | -61.18      | 321       |
| Endocyte ECYT      |        | 14.59     | 12.01      | -17.68     | 55.37       | 591       |
| Entremed ENMD      |        | 2.27      | 2.05       | -9.69      | -59.65      | 583       |
| Enzo Biochem       | ENZ    | 4.71      | 4.28       | -9.13      | -21.18      | 885       |
| Enzon Pharma       | ENZN   | 10.23     | 10.26      | 0.29       | -15.90      | 1366      |
| Epicept EPCT       |        | 0.52      | 0.54       | 3.85       | -36.47      | 107       |
| Exelixis EXEL      |        | 9.12      | 8.89       | -2.52      | 3.49        | 5007      |
| Flamel Tech        | FLML   | 5.44      | 5.13       | -5.70      | -26.29      | 82        |
| Forest Labs        | FRX    | 39.37     | 38.46      | -2.31      | 20.30       | 12244     |
| Furiex Pharma      | FURX   | 17.81     | 18.01      | 1.12       | 24.64       |           |
| Generex Biotech    | GNBT   | 0.22      | 0.14       | -36.36     | -52.53      | 13618     |
| Genomic Health     | GHDX   | 28.5      | 27.37      | -3.96      | 25.09       | 305       |
| GenVec GNVV        |        | 3.27      | 3.14       | -3.98      | 450.88      | 541       |
| Geron GERN         |        | 4.39      | 4.03       | -8.20      | -22.65      | 6682      |
| Gilead Sciences    | GILD   | 42.44     | 41         | -3.39      | 13.07       | 29769     |
| GTx GTXI           |        | 4.8       | 4.66       | -2.92      | 68.84       | 790       |
| Harbor Biosci      | HRBR   | 0.22      | 0.2        | -9.09      | 53.85       | 125       |
| Harvard Bio        | HBIO   | 6         | 5.66       | -5.67      | 39.41       | 607       |
| Human Genome       | HGSI   | 24.52     | 23.2       | -5.38      | -4.13       | 10628     |
| Idenix Pharma      | IDIX   | 5.4       | 6.08       | 12.59      | 21.84       | 3100      |
| Idera Pharma       | IDRA   | 1.9       | 1.93       | 1.58       | -33.45      | 86        |
| ImmunoGen IMGN     |        | 14.15     | 15.4       | 8.83       | 63.48       | 3876      |
| Immunomedics IMMU  |        | 4.18      | 4.13       | -1.20      | 14.72       | 2180      |
| Incyte INCY        |        | 19.82     | 20.07      | 1.26       | 19.68       | 6966      |

| Company             | Symbol | Close 7/8 | Close 7/15 | %Change WK | %Change YTD | Vol (000) |
|---------------------|--------|-----------|------------|------------|-------------|-----------|
| Infinity Pharma     | INFI   | 8.05      | 9.16       | 13.79      | 51.40       | 347       |
| Inhibifex INHX      |        | 3.93      | 3.99       | 1.53       | 48.33       | 2338      |
| InterMune ITMN      |        | 36.74     | 37.01      | 0.73       | 0.27        | 4541      |
| Ironwood Pharma     | IRWD   | 16.04     | 15.79      | -1.56      | 52.56       | 820       |
| ISIS Pharma         | ISIS   | 9.31      | 9.12       | -2.04      | -10.15      | 1681      |
| Keryx Biopharma     | KERX   | 4.94      | 4.91       | -0.61      | 5.14        | 3058      |
| Labopharm DDSF      |        | 0.2       | 0.16       | -20.00     | -83.16      | 216       |
| Lexicon LXR         |        | 1.67      | 1.75       | 4.79       | 17.45       | 4014      |
| Ligand Pharma       | LGND   | 11.68     | 11.55      | -1.11      | 29.63       | 545       |
| MannKind MNKD       |        | 3.86      | 3.66       | -5.18      | -54.98      | 2575      |
| Map Pharma          | MAPP   | 16        | 16.04      | 0.25       | -3.72       | 524       |
| Maxygen MAXY        |        | 5.48      | 5.47       | -0.18      | 38.83       | 691       |
| MDRNa MRNA          |        | 0.23      | 0.2        | -13.04     | -86.92      | 21832     |
| Metabolix Inc.      | MBLX   | 6.86      | 6.81       | -0.73      | -42.77      | 874       |
| Micromet MITI       |        | 5.76      | 6.29       | 9.20       | -23.94      | 6412      |
| Momenta Pharma      | MNTA   | 20.68     | 19.51      | -5.66      | 29.89       | 1835      |
| Myrex MYRX          |        | 3.6       | 3.56       | -1.11      | -16.24      | 450       |
| Myriad Genetics     | MYGN   | 23.26     | 23.56      | 1.29       | 2.75        | 4243      |
| Nabi Biopharma      | NABI   | 5.51      | 5.63       | 2.18       | -3.76       | 1047      |
| Nanogen NGEN        |        | 0.01      | 0.01       | 0.00       | 17.65       | 269       |
| Nektar Therap       | NKTR   | 7.52      | 7.65       | 1.73       | -40.97      | 5791      |
| NeoPharma NEOL      |        | 0.35      | 0.33       | -5.71      | 13.79       | 485       |
| Neurocrine Biosci   | NBIX   | 8.4       | 8.02       | -4.52      | 4.29        | 917       |
| NeurogesX NGSX      |        | 1.63      | 1.7        | 4.29       | -73.10      | 640       |
| NovaBay NBY         |        | 1.02      | 1.05       | 2.94       | -37.13      | 320       |
| Novavax NV          | AX     | 1.96      | 1.96       | 0.00       | -23.14      | 1827      |
| NPS Pharma          | NPSP   | 10.18     | 9.91       | -2.65      | 23.57       | 2867      |
| NuPathe P           | ATH    | 7.49      | 7.29       | -2.67      | -19.54      | 391       |
| Omeros OMER         |        | 4.21      | 4.14       | -1.66      | -50.48      | 174       |
| OncoGenex Pharma    | OGXI   | 17.2      | 15.83      | -7.97      | -3.77       | 151       |
| Oncothyreon ONTY    |        | 8.54      | 8.1        | -5.15      | 147.71      | 5881      |
| Onyx Pharma         | ONXX   | 36.58     | 34.66      | -5.25      | -6.20       | 4818      |
| Opko Health         | OPK    | 4.06      | 4.3        | 5.91       | 15.90       | 7865      |
| Optimer Pharma      | OPTR   | 12.04     | 11.42      | -5.15      | -0.70       | 1764      |
| OraSure Tech        | OSUR   | 9.93      | 9.82       | -1.11      | 64.49       | 813       |
| Ore Pharma          | ORXED  | 0.14      | 0.15       | 7.14       | -39.02      | 1         |
| Orexigen OREX       |        | 1.67      | 1.68       | 0.60       | -79.41      | 2433      |
| Osiris Thera        | OSIR   | 7.98      | 7.95       | -0.38      | 0.13        | 532       |
| Oxis International  | OXIS   | 0.1       | 0.08       | -20.00     | -40.74      | 689       |
| Pacific Biosciences | PACB   | 12.01     | 11.09      | -7.66      | -30.30      | 902       |
| Pacira Pharma       | PCRX   | 11.92     | 11.46      | -3.86      | 63.25       | 290       |
| Pain Therapeutics   | PTIE   | 4.64      | 4.61       | -0.65      | -31.09      | 3988      |
| Palatin Tech        | PTN    | 1.09      | 1.05       | -3.67      | -18.60      | 1730      |
| Panacos Pharma      | PANC   | 0.01      | 0          | -100.00    | -100.00     | 147       |
| Peregrine Pharma    | PPHM   | 1.97      | 1.88       | -4.57      | -14.55      | 3125      |
| Pharma Prdt Dev     | PPDI   | 27.87     | 27.86      | -0.04      | 1.27        | 3967      |
| Pharmacyclics PCYC  |        | 11.54     | 12.13      | 5.11       | 94.39       | 6110      |
| Pharmasset VRUS     |        | 127.91    | 125.54     | -1.85      | 185.71      | 1888      |
| Pharmos P           | ARS    | 0.12      | 0.12       | 0.00       | 20.00       | 14        |
| Poniard Pharma      | PARD   | 0.23      | 0.21       | -8.70      | -63.79      | 256       |
| Pozen POZN          |        | 4.59      | 4.58       | -0.22      | -30.29      | 597       |
| Progenics Pharma    | PGNX   | 7.63      | 7.37       | -3.41      | 36.23       | 264       |
| Protalix Biothera   | PLX    | 6.68      | 6.79       | 1.65       | -31.96      | 1910      |
| Protein Design      | PDLI   | 5.75      | 6.26       | 8.87       | 0.64        | 19629     |
| Qiagen QGEN         |        | 19.17     | 18.28      | -4.64      | -6.02       | 8674      |
| QLT Inc.            | QLTI   | 7.31      | 7.09       | -3.01      | -0.98       | 461       |
| Raptor Pharma       | RPTP   | 6.28      | 6.54       | 4.14       | 79.67       | 3457      |
| Regeneron Pharma    | REGN   | 59.64     | 55.59      | -6.79      | 66.54       | 2797      |
| Repligen RGEN       |        | 3.53      | 3.71       | 5.10       | -21.51      | 301       |
| Rexahn Pharma       | RNN    | 1.22      | 1.26       | 3.28       | 9.57        | 2642      |
| Rigel Pharma        | RIGL   | 9.9       | 10.15      | 2.53       | 33.55       | 2244      |
| Rosetta Genomics    | ROSGD  | 1.16      | 1.54       | 32.76      | 62.11       | 1067      |
| Rxi Pharma          | RXII   | 1.22      | 1.28       | 4.92       | -51.52      | 9030      |
| Sagent Pharma       | SGNT   | 25.93     | 23.97      | -7.56      | 24.91       | 299       |
| Sangamo Biosci      | SGMO   | 6.26      | 5.98       | -4.47      | -12.83      | 2397      |
| Santarus SNTS       |        | 3.36      | 3.27       | -2.68      | -0.61       | 774       |
| Savient Pharma      | SVNT   | 7.47      | 7.72       | 3.35       | -31.26      | 6545      |
| SciClone Pharma     | SCLN   | 6.21      | 6.41       | 3.22       | 51.18       | 2003      |
| Seattle Genetics    | SGEN   | 21.08     | 18.87      | -10.48     | 23.01       | 19266     |
| Sequenom SQNM       |        | 7.82      | 7.55       | -3.45      | -7.25       | 6433      |
| SIGA Tech           | SIGA   | 9.26      | 8.8        | -4.97      | -36.96      | 3387      |
| Somaxon Pharma      | SOMX   | 1.85      | 1.6        | -13.51     | -50.16      | 3039      |
| Spectrum Pharma     | SPPI   | 10.05     | 10.63      | 5.77       | 50.14       | 7624      |
| StemCells STEM      |        | 6.08      | 4.51       | -25.82     | 306.31      | 450       |
| Sucampo Pharma      | SCMP   | 4.09      | 4.13       | 0.98       | 7.83        | 84        |
| SuperGen SUPG       |        | 3.16      | 3.01       | -4.75      | 14.02       | 2334      |
| Synta Pharma        | SNTA   | 5.11      | 4.95       | -3.13      | -19.12      | 959       |
| Talon Thera         | TLON   | 0.95      | 1          | 5.26       | 108.33      | 322       |
| Targacept           | TRGT   | 21.35     | 21.95      | 2.81       | -17.76      | 830       |
| Telik TELK          |        | 0.63      | 0.64       | 1.59       | -20.50      | 170       |
| Tengion TNGN        |        | 1.16      | 1.33       | 14.66      | -51.46      | 373       |

| Company             | Symbol | Close 7/8 | Close 7/15 | %Change WK | %Change YTD | Vol (000) |
|---------------------|--------|-----------|------------|------------|-------------|-----------|
| Theravance THR      |        | 24.23     | 24.18      | -0.21      | -5.36       | 1713      |
| Titan Pharma        | TTNP   | 1.76      | 1.95       | 10.80      | 59.84       | 2930      |
| Transcept Pharma    | TSPT   | 7.98      | 4.87       | -38.97     | -35.50      | 4848      |
| Transgenomic TBIO   |        | 1.76      | 1.65       | -6.25      | 132.39      | 264       |
| Tranzyme TZYM       |        | 4.28      | 4.12       | -3.74      | 3.00        | 47        |
| Trimeris TRMS       |        | 2.48      | 2.52       | 1.61       | 3.28        | 2311      |
| Trinity Biotech     | TRIB   | 10.04     | 10.06      | 0.20       | 13.80       | 351       |
| Trius Therap        | TSRX   | 7.41      | 7.82       | 5.53       | 116.32      | 192       |
| Unigene UGNE        |        | 1.01      | 1.2        | 18.81      | 79.10       | 356       |
| United Therap       | UTHR   | 55.33     | 56.22      | 1.61       | -11.23      | 4797      |
| Vanda Pharma        | VNDA   | 7.28      | 7.15       | -1.79      | -23.77      | 771       |
| Ventrus Biosciences | VTUS   | 13.47     | 12.96      | -3.79      | 95.77       | 1315      |
| Vermillion VRML     |        | 3.86      | 3.94       | 2.07       | -46.90      | 626       |
| Vertex Pharma       | VRTX   | 50.67     | 50.68      | 0.02       | 43.41       | 7887      |
| Vical VICL          |        | 4.42      | 4.61       | 4.30       | 124.88      | 4971      |
| ViroPharma VPHM     |        | 19.99     | 19.34      | -3.25      | 9.89        | 3495      |
| Vivus VVUS          |        | 8.41      | 8.34       | -0.83      | -12.49      | 5847      |
| XenoPort XNPT       |        | 7.65      | 7.48       | -2.22      | -13.63      | 1428      |
| Zaliscus Inc        | ZLCS   | 2.76      | 2.61       | -5.43      | 60.12       | 10169     |
| Zogenix ZGNX        |        | 4.47      | 5.03       | 12.53      | -11.29      | 374       |

**LONDON STOCK EXCHANGE**

| Company          | Symbol | 7/8   | 7/15  | %WK   | %YTD   | Volume |
|------------------|--------|-------|-------|-------|--------|--------|
| Antisoma ASM     |        | 2.71  | 2.47  | -8.86 | -92.52 | 23593  |
| Ark Therapeutics | AKT    | 5.28  | 4.925 | -6.64 | -64.95 | 2759   |
| Asterand A       | TD     | 10.5  | 10    | -4.76 | -46.24 | 296    |
| Oxford Biomedica | OXB    | 6.8   | 6.96  | 2.35  | -38.13 | 13226  |
| Phytopharm PYM   |        | 7.88  | 7.6   | -3.60 | -29.89 | 728    |
| Puricare         | PURI   | 35.15 | 36.5  | 3.84  | 172.39 | 4      |
| Renovo Group     | RNVO   | 14    | 14.25 | 1.79  | -50.69 | 2276   |
| SkyePharma SKP   |        | 41.6  | 43    | 3.37  | -49.98 | 38     |
| Vernalis plc     | VER    | 39.79 | 39.5  | -0.72 | -54.60 | 55     |

Note: Prices are denoted in pence.

**TORONTO STOCK EXCHANGE**

| Company             | Symbol | 7/8  | 7/15 | %WK    | %YTD   | Volume |
|---------------------|--------|------|------|--------|--------|--------|
| Adherex Technol     | AHX    | 0.04 | 0.04 | 0.00   | -11.11 | 142    |
| Allon Therapeutics  | NPC    | 0.37 | 0.36 | -2.70  | 12.50  | 99     |
| BELLUS Health       | BLU    | 0.06 | 0.06 | 0.00   | -66.67 | 480    |
| Bioniche Life Sci   | BNC    | 0.96 | 0.9  | -6.25  | 60.71  | 237    |
| Cangene             | CNJ    | 1.56 | 1.57 | 0.64   | -69.22 | 39     |
| Isotechnika         | ISA    | 0.16 | 0.14 | -12.50 | -15.15 | 118    |
| Lorus Therapeutics  | LOR    | 0.45 | 0.44 | -2.22  | 576.92 | 20     |
| Medicago            | MDG    | 0.47 | 0.47 | 0.00   | -29.85 | 0      |
| MethylGene          | MYG    | 0.34 | 0.35 | 2.94   | 25.00  | 483    |
| Oncolytics Biotech  | ONC    | 5.04 | 4.61 | -8.53  | 67.64  | 507    |
| Protex Therapeutics | PRX    | 0.51 | 0.54 | 5.88   | -36.47 | 405    |
| Resverlogix         | RVX    | 1.48 | 1.48 | 0.00   | -38.84 | 141    |
| SemBioSys Gen       | SBS    | 0.06 | 0.07 | 16.67  | -65.00 | 54     |
| Tekmira Pharma      | TKM    | 2.35 | 2.25 | -4.26  | 141.94 | 39     |
| Thallion Pharma     | TLN    | 0.16 | 0.15 | -6.25  | 36.36  | 502    |
| Theratechnologies   | TH     | 4.5  | 4.22 | -6.22  | -4.74  | 623    |
| Wex Pharma          | WXI    | 0.15 | 0.15 | 0.00   | -9.09  | 0      |
| YM BioSciences      | YM     | 2.6  | 2.65 | 1.92   | 82.76  | 80     |

Note: Prices are denoted in Canadian dollars.

**NOTES:**

Trading volumes for Nasdaq, Amex and NYSE are recorded as the total number of shares traded (in thousands) on a weekly basis (cumulative Monday through Friday); the weekly and YTD % changes are from IPO completion, where applicable.

**Average Percent Change Week: -2.07%**

Range: -38.97% to +32.76%; Number Of Companies: 210 (does not include LSE or TSX; not market weighted)

**Average Percent Change YTD: +11.93%**

Range: -88.89% to +450.88%; Number Of Companies: 210 (does not include LSE or TSX; not market weighted)