

Revisiting Transcept

## Reverse Merger Returns Vary Widely: Weighing the Risk

By Trista Morrison  
Editor

Investors in Novacea Inc. prior to its reverse merger with Transcept Pharmaceuticals Inc. three years ago might be forgiven for saying, "I told you so."

At the time of the deal, Novacea was sitting on about \$90 million left over after the Phase III failure of prostate cancer drug Asentar. It was rumored that nearly 100 privately held biotechs vied for a chance to reverse merge with the cash shell, and Transcept won out – much to the dismay of Novacea's investors.

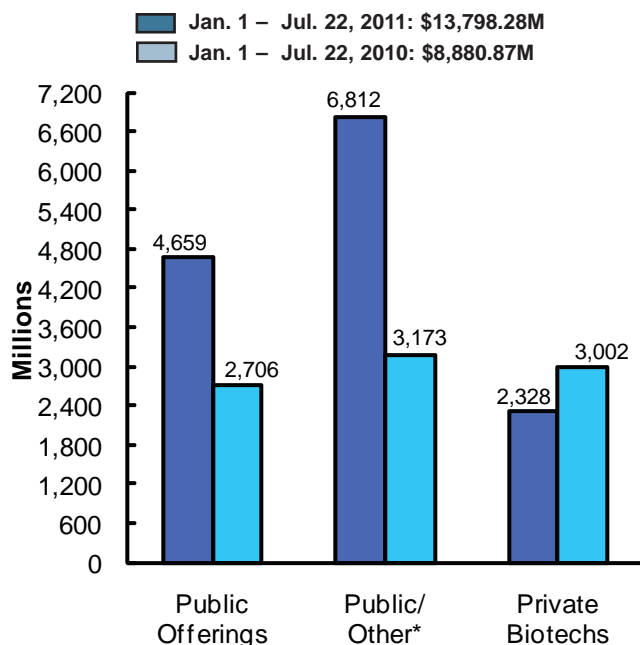
On the conference call announcing the deal, Novacea investors complained that the firm was giving away its cash to an entity that still had to face an increasingly cautious FDA with a product that lacked external validation. They raised concerns about cross-ownership issues, called the deal "very, very bad for the company's public shareholders," and pushed the stock down 24.3 percent. (See *BioWorld Today*, Sept. 3, 2008.)

Now that the FDA has issued a second complete response letter for Transcept's insomnia drug Intermezzo (zolpidem tartrate), it looks like investors were right to be concerned. (See *BioWorld Today*, July 14, 2011.)

According to a *BioWorld Insight* analysis, the stock is now down 69 percent from where it was just after Novacea's Asentar imploded. And Novacea was trading below its cash value at the time; the decline from what investors would have received had Novacea liquidated back then versus what their Transcept shares are worth today is 77 percent. (See the chart on page 7.)

But the deal wasn't bad for everyone involved. In fact, comparing the market capitalization of the merged entity just

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.

after the deal closed to the current market cap shows a 34 percent increase in value, even after the Intermezzo complete response letter. Running the numbers before that recent setback would have shown a whopping 238 percent value creation.

### Success Versus Failure

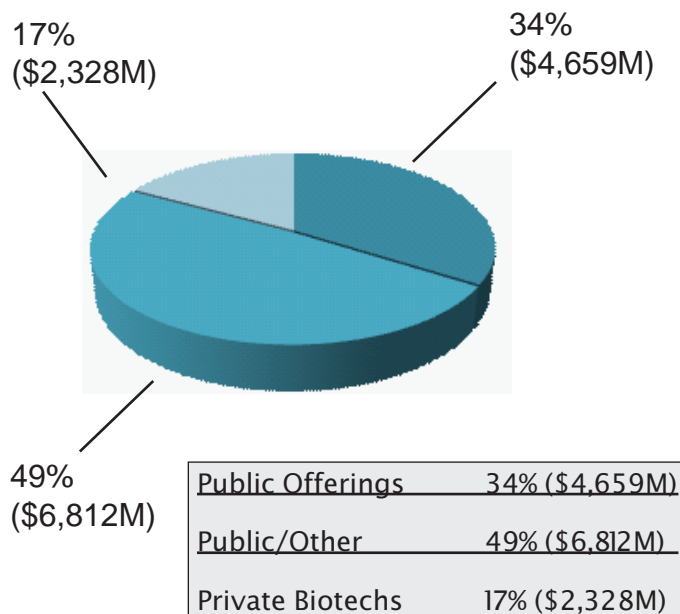
There are some reverse mergers that look good in every light. Cougar Biotechnology Inc. is the biotech example

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## Money Raised By Biotech: Jan. 1 - Jul. 22, 2011



## Reverse Mergers

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most-often cited: The firm reversed merged with shell SRKP 4 Inc. back in 2006, saw its stock rocket 150 percent in three years thanks to good data for prostate cancer drug abiraterone acetate, and was sold to Johnson & Johnson for nearly \$1 billion. (See *BioWorld Today*, April 10, 2006, and May 26, 2009.)

More recently, there was OncoGenex Pharmaceuticals Inc., which went public in 2008 via a reverse merger with Sonus Pharmaceuticals Inc. following the Phase III failure of Sonus' Tocosol Paclitaxel. Thanks to great data with OncoGenex's antisense pipeline, including lead drug custirsen for prostate cancer, the merged firm has seen nearly a 1,600 percent increase in market cap, and even original Sonus investors have seen a positive return. (See *BioWorld Today*, May 29, 2008, and Dec. 22, 2009.)

But such glowing examples are scarce. On the whole, biotech reverse mergers tend to be a bad deal for investors in the public shell. That's why, in recent years, investors have fought such transactions. Investor pressure put the kibosh on a proposed 2009 merger between Australian biotechs Progen Pharmaceuticals Ltd. and Avexa Ltd., while Deerfield Management prevented shell firm NitroMed Inc. merging with Archemix Inc. Shareholders of VaxGen Inc. voted down two reverse merger proposals – one with Raven Biotechnologies Inc. and another with Oxigene Inc. – before finally agreeing to merge with diaDexus Inc. (See *BioWorld Insight*, Feb. 28, 2011.)

Whether or not reverse mergers are good for investors

in the new merged entity is hit or miss: market caps tend to go either way up or way down.

Steven Bronson, founder, chairman and CEO of investment banking firm Catalyst Financial LLC, said the success of a reverse merger is driven by two factors. The first, and most important, is "execution of the business model," he said. The shell company is making a bet that the technology being developed by the private firm will work, and in the biotech industry, that's always a risky bet.

So you have outcomes like ARCA Biopharma Inc., which reverse-merged with Nuvelo Inc. after the failure of Nuvelo's clot-busting drug alimeprase. Shares of Nuvelo gained when the merger was announced, perhaps because ARCA's beta-blocker Gencaro (bucindolol) was already under FDA review for heart failure. But the FDA slapped Gencaro with a complete response letter requesting another trial, and shares plummeted. (See *BioWorld Today*, Sept. 26, 2008, and March 12, 2010.)

The second factor Bronson cited as critical to the success of a reverse merger is sponsorship. Unlike initial public offerings (IPO), reverse mergers don't involve investment bankers trotting management around to meet with institutional investors, raising awareness and creating a shareholder base. Thus, like firms that go public on a foreign exchange and then transfer to the OTCBB, or those that go public via the Form 10 pathway, visibility and volume can be very low at first.

But "ultimately, it's about the success of the business," Bronson said.

Annette Grimaldi, managing director with BMO Capital Markets Corp., agreed. The most important thing management teams of the shell company can do to ensure the success of the reverse merger is extensive due diligence, she said, adding "the key is choosing to combine with a company that has a good chance."

## Drawbacks Versus Benefits

By that logic, reverse mergers, despite their bad reputation, might not necessarily be more doomed to failure than any other biotech investment. Yet Grimaldi noted that, historically, some private companies have opted for reverse mergers because they were not strong enough for a traditional IPO, resulting in poor aftermarket performance as a result of negative selection bias rather than a problem inherent in the reverse merger structure.

Reverse mergers do come laden with their own, unique baggage. Many failed biotech shells have disgruntled shareholders who may not be interested in the private company, and it takes time for them to cycle out of the stock. Shells also tend to have a largely retail shareholder base, and it takes not only time, but adequate price appreciation and volume to attract institutions. There's also the lack of sponsorship and requirement of shareholder approval, as previously noted, and the fact that the shell might have

*See Reverse Mergers, page 6*

## WORD ON THE STREET

“There were no benefits of a reverse merger not offset by the drawbacks.”

– *Fran Stoller, partner with law firm Loeb & Loeb LLP, which advised Coronado Biosciences Inc. on filing a Form-10 rather than pursuing a reverse merger*

“I realize it’s absurd to talk about 10Xs or even 5Xs these days.”

– *Roger Longman, CEO of Real Endpoints LLC*

“To get competition [in drug pricing], you have to pick winners or losers.”

– *Jonathan Blum, Medicare deputy administrator and director at CMS, speaking at a hearing of the Senate Special Committee on Aging*

“It’s the dream that the next experiment probably won’t work, but it might.”

– *Jim Greenwood, BIO president and CEO, on what keeps bio pushing against the odds*

## WEEK IN WASHINGTON

The FDA issued a proposed guidance laying out a tentative regulatory pathway for companion diagnostics. The agency also issued a draft guidance on mobile medical apps.

The Centers for Medicare & Medicaid Services is taking the first steps to develop a national benchmark that states can use to set prescription drug reimbursement.

## Reverse Mergers

*Continued from page 4*

debts or other liabilities.

Reverse mergers will also soon face new hurdles from Nasdaq. The exchange has filed three proposals that would result in more stringent listing requirements for firms that go public through the reverse merger process.

First, reverse merger firms will not be eligible to apply for Nasdaq listing until six months after the merged entity submits audited financial statements to the SEC. Second, the merged company’s stock must have a closing bid price of \$4 or more for at least 30 of the 60 trading days immediately preceding the application for Nasdaq listing. Third, at least two financial reports related to the combined entity must be filed with the SEC prior to listing on Nasdaq.

The proposals are under review at the SEC. Although they arose from recent problems with sketchy Chinese companies using reverse mergers to gain a U.S. listing, Nasdaq spokespersons said they would apply to all reverse mergers in the future. That includes private biotechs that merge into a Form-10 shell or an OTC-listed shell with the intention of transferring to Nasdaq, although the changes would not impact biotechs that merge into a Nasdaq-listed shell.

Despite the many challenges, there are benefits to reverse mergers as well. In a recent research note, Grimaldi wrote that reverse mergers are less susceptible to market conditions than IPOs, and that the separation of the listing process from a financing gives the company more financing

*See Reverse Mergers, page 7*

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## Reverse Mergers

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flexibility. Indeed, in the biotech world, many shells bring a hefty cash balance to the table, removing the need for subsequent financing in the short term.

### Then Versus Now

For these are other reasons, reverse mergers continue to be a popular strategy in biotech, with plenty of firms hoping to be the next Cougar or OncoGenex.

Last month, private firm Allozyne Inc. announced plans to merge with struggling Nasdaq-listed biotech Poniard Pharmaceuticals Inc., while Synageva BioPharma Corp. moved to reverse merge with Nasdaq-listed Trimeris Inc. (See *BioWorld Today*, June 14, 2011, and June 24, 2011.)

Earlier this year, Radius Health Inc. said it had begun the process of going public through a reverse merger with unregistered MPM Acquisition Corp. VistaGen Therapeutics Inc. inked a deal to merge with OTCBB-listed Excaliber Enterprises Ltd., and IntelliCell Biosciences Inc. announced plans to merge with OTCBB-listed Media Exchange Group. Can-Fite BioPharma Ltd. also agreed to spin off its ophthalmic indications in a reverse merger deal with OTCBB-listed Denali Concrete Management Inc. (See *BioWorld Today*, May 25, 2011.)

Late last year, Pathfinder LLC decided to go public via a reverse merger with OTCBB-listed SyntheMed Inc., Genesis Biopharma Inc. went public through a reverse merger with OTCBB-listed Freight Management Co. and Insys Therapeutics Inc. reverse merged with Pink Sheets-listed NeoPharm Inc.

As long as the IPO window remains largely closed, biotechs will likely continue to pursue alternative pathways to public listing, such as reverse mergers and Form-10 filings. (See a related story in this issue.) And as long as biotechs continue to have a high failure rate, there should be no shortage of publicly listed biotech shells for private firms to merge into.

Perhaps even Transcept, which itself went public via a reverse merger with a shell, could one day wind up serving as a shell for the next private biotech seeking a public listing. As of now, Transcept has said it is continuing to pursue a path forward for Intermezzo and develop TO-2061, a low-dose formulation of ondansetron that recently began Phase II trials as an adjunctive for obsessive compulsive disorder.

But Transcept does have a Nasdaq listing, not to mention \$59.6 million of cash, equivalents and marketable securities as of June 30. That package probably looks pretty enticing to many private biotechs finding themselves running on venture fumes and shut out of the IPO window. ■

## Performance of Select 2007-2008 Biotech Reverse Mergers

| Public Shell                 | Private Co.                         | Stock price after implosion*       | Cash/share just after implosion** | Stock price after merger announced* | Cash/share at merger   | Market Cap 30 days after merger close*** | Stock price 07/19/11 | Market Cap 07/19/11 | Change in stock price since implosion | Change in market cap since merger |
|------------------------------|-------------------------------------|------------------------------------|-----------------------------------|-------------------------------------|------------------------|--|----------------------|---------------------|---------------------------------------|-----------------------------------|
| Cellegy Pharmaceuticals Inc. | Adamis Pharmaceuticals Corp.        | 45 cents (\$4.47 adj) [07/10/2006] | 3 cents (30 cents adj)            | 8 cents (79 cents adj) [2/13/2008]  | 3 cents (30 cents adj) | \$3.5M                                   | 24 cents             | \$19.95M            | (94.5%)                               | 470%                              |
| Critical Therapeutics Inc.   | Cornerstone BioPharma Holdings Inc. | \$1.92 (\$19.20 adj) [11/8/2007]   | 79 cents (\$7.90 adj)             | 48 cents (\$4.80 adj) [5/1/2008]    | 25 cents (\$2.50 adj)  | \$42.9M                                  | \$8.76               | \$213M              | (54.4%)                               | 396.5%                            |
| Novacea Inc.                 | Transcept Pharmaceuticals Inc.      | \$2.89 (\$14.45 adj) [11/5/2007]   | \$3.92 (\$19.60 adj)              | \$1.78 (\$8.90 adj) [9/2/2008]      | \$3.46 (\$17.30 adj)   | \$43.6M                                  | \$4.43               | \$58.6M             | (69.3%)                               | 34.4%                             |
| Nuvelo Inc.                  | ARCA Biopharma Inc.                 | \$4.05 (\$81 adj) [12/11/2006]     | \$2.88 (\$57.60 adj)              | 42 cents (\$8.40 adj) [9/25/2008]   | \$1.10 (\$22 adj)      | \$40.8M                                  | \$1.62               | \$16.9M             | (98%)                                 | (58.6%)                           |
| Point Therapeutics Inc.      | Dara Biosciences Inc.               | 40 cents (\$16 adj) [03/1/2007]    | 22 cents (\$8.80 adj)             | 26 cents (\$10.40 adj) [10/9/2007]  | 5 cents (\$2 adj)      | \$80.9M                                  | \$2.59               | \$13.44M            | (83.8%)                               | (83.4%)                           |
| Sonus Pharmaceuticals Inc.   | OncoGenex Technologies Inc.         | 70 cents (\$12.60 adj) [9/24/2007] | \$1.10 (\$19.80 adj)              | 28 cents (\$5.04 adj) [5/27/2008]   | 63 cents (\$11.34 adj) | \$9.1M                                   | \$16.07              | \$154.6M            | 27.5%                                 | 1,599%                            |

\*Stock price based on article in *BioWorld Today*. Adjusted figure accounts for reverse stock splits subsequent to close of merger.

\*\*Based on cash and share data in quarterly filing following implosion. Adjusted figure accounts for reverse stock splits.

\*\*\*Data from BMO Capital Markets Corp.

## Top 10 Bio/Pharma Deals This Year

| Companies                           | Month    | Amount   |
|-------------------------------------|----------|----------|
| AVEO Pharmaceuticals/Astellas       | February | \$1.425B |
| Rib-X Pharmaceuticals/Sanofi SA     | July     | \$763M   |
| Intra-Cellular Therapies/Takeda     | March    | \$750M   |
| Epizyme/GlaxoSmithKline             | January  | \$650M   |
| Theraclone Sciences/Pfizer          | Januray  | \$632M   |
| Santaris Pharma/Pfizer              | January  | \$614M   |
| Glenmark Pharma/Sanofi-Aventis      | May      | \$613M   |
| Astellas Pharma/Royalty Pharma      | July     | \$609M   |
| AVEO/Centocor Ortho                 | June     | \$555M   |
| Zealand Pharma/Boehringer Ingelheim | June     | \$537.3M |

## Collaborations Between Biotech And Pharmaceutical Companies: June 1 - July 22, 2011

**TOTAL VALUE IN 2011: \$13,545.95M\***

NUMBER OF DEALS IN 2011: 143

| Company (Location)   | Company (Location)  | Value (M) | Type/Product Area  | Terms/Details (Date)   |
|--|---|-----------|--|--|
| <b>JUNE</b>  |   |           |  |  |
| <b>Affectis Pharmaceuticals AG</b><br>(Munich, Germany)    | Merck Serono (division of Merck KgaA; Darmstadt, Germany)             | \$407.5   | Deal to develop neurology compounds targeting P2X7 receptors, a calcium channel thought to play a role in neuroprotection  | The deal gives Merck worldwide rights to develop and commercialize the compounds in exchange for \$3.5M up front, plus research funding, with a potential \$404M in milestones, plus royalties (6/9) |
| <b>Audion Therapeutics</b><br>(Amsterdam, the Netherlands) | Sanofi-Aventis SA (Paris)   | ND        | Two-year research collaboration to develop potential treatments for hearing loss through the optimization of small molecules by using a regenerative medicine approach | Sanofi has an option to license technology rights from Audion (6/17)   |
| <b>AVEO Pharmaceuticals Inc.</b><br>(Cambridge, Mass.)     | Centocor Ortho Biotech Inc. (Horsham, Pa.; unit of Johnson & Johnson) | \$555     | Exclusive worldwide development and commercialization deal to AVEO's preclinical antibodies targeting the RON receptor   | Centocor paid \$15M up front, and will pay as much as \$540M in milestones, plus double-digit royalties on worldwide net sales (6/1)   |
| <b>BioMarin Pharmaceutical Inc.</b><br>(Novato, Calif.)    | Pfizer Inc. (New York)  | \$48.5    | Purchase of a bulk biologics manufacturing plant in Cork, Ireland from Pfizer  | BioMarin paid \$48.5M for the plant, which will produce enzyme replacement therapy GALNS, as well as other products (6/24)   |

| Company (Location)                                  | Company (Location)   | Value (M) | Type/Product Area  | Terms/Details (Date)   |
|---|--|-----------|--|--|
| <b>BioPontis Alliance LLC</b> (Raleigh, N.C.)       | Janssen Biotech Inc. (Horsham, Pa.; formerly Centocor Ortho Biotech Inc.; part of Johnson & Johnson) | ND        | Translational Research Agreement for drug development  | BioPontis will receive input and guidance to ensure its early programs are aligned with market demand; Janssen will have access to evaluate and license early stage therapeutic opportunities (6/30) |
| <b>Biotech AG</b> (Dreieich, Germany)               | Abbott (Abbott Park, Ill.)   | \$480     | Autoimmune disease deal focused on BT-061 for rheumatoid arthritis and psoriasis   | Biotech gets \$85M up front and is eligible for \$395M in milestones, plus royalties on worldwide sales, except in Europe, where the companies will co-promote BT-061 (6/22)                         |
| <b>Clovis Oncology Inc.</b> (Boulder, Colo.)        | Pfizer Inc. (New York)   | \$255     | Deal for the right to develop and commercialize PF-01367338, an inhibitor of Poly ADP-ribose polymerase inhibitor, which is in Phase I/II development for solid tumors | Clovis will pay an undisclosed up-front fee to Pfizer, plus potential milestones of \$255M; Pfizer Venture Investments will make an equity investment in Clovis (6/6)                                |
| <b>Clovis Oncology Inc.</b> (Boulder, Colo.)        | Roche AG (Basel, Switzerland)  | ND        | Partnership to develop a PCR-based companion diagnostic test for epidermal growth factor receptor mutations in non-small-cell lung cancer                              | The test is being developed to support CO-1686, which targets the T790M mutant form of EGFR (6/3)  |
| <b>Cortex Pharmaceuticals Inc.</b> (Irvine, Calif.) | Servier (Paris)  | \$1       | Agreement to sell rights to CX1632 to Servier for an up-front payment of \$1M  | The companies will remain joint owners of related patents; in the event that Servier opts to acquire sole ownership of patent rights to CX1632, it will pay Cortex an additional \$2M (6/14)         |
| <b>Evotec AG</b> (Hamburg, Germany)                 | Roche AG (Basel, Switzerland)  | ND        | Collaboration to identify appropriate pharmacodynamics and protein-activity-based patient stratification biomarkers for Roche's oncology drugs                         | Evotec will use its phospho-Scout platform to discover protein-phosphorylations, while Roche will conduct clinical trials and assess the development of companion diagnostics (6/27)                 |
| <b>Gilead Sciences Inc.</b> (Foster City, Calif.)   | Johnson & Johnson (New Brunswick, N.J.)  | ND        | License agreement to develop and commercialize a fixed-dose combination of Gilead's Phase III boosting agent cobicistat and Tibotec's Prezista for HIV                 | Tibotec will be responsible for the formulation, manufacturing, registration, distribution and commercialization of the combination product worldwide (6/29)   |

| Company (Location)   | Company (Location)  | Value (M) | Type/Product Area   | Terms/Details (Date)   |
|--|---|-----------|---|--|
| <b>Hanwha Chemical Corp.</b> (Seoul, South Korea)          | Merck and Co. Inc. (Whitehouse Station, N.J.)                       | ND        | Development and commercialization agreement for a biosimilar form of Enbrel   | Merck made an undisclosed up-front payment to Hanwha, with possible additional milestone payments and tiered royalties on product sales (6/14)   |
| <b>Heptares Therapeutics Ltd.</b> (Welwyn Garden City, UK) | AstraZeneca plc (London)  | \$6.25    | Four-year collaboration focused on discovery and development of new medicines for the treatment of central nervous system, metabolic and other diseases targeting G-protein coupled receptors       | Heptares will receive an up-front \$6.25M cash payment plus committed research funding and potential milestone payments and royalties (6/1)  |
| <b>Neuralstem Inc.</b> (Rockville, Md.)                    | Summit Pharmaceuticals International Corp. (Tokyo)                  | ND        | Licensing agreement for its depression candidate, NSI-189   | The agreement gives SPI the right to market development and licensing rights to the drug (6/8)   |
| <b>PTC Therapeutics Inc.</b> (South Plainfield, N.J.)      | AstraZeneca plc (London)  | ND        | Partnership for its Gene Expression Modulation by Small-molecules drug discovery platform; initially focused on oncology but could encompass up to eight targets across different therapeutic areas | PTC will get an undisclosed amount of money from an up-front cash payment, committed research funding, milestone payments and royalties; PTC has an option to participate in the development of select product candidates (6/30) |
| <b>Sirnaomic Inc.</b> (Gaithersburg, Md.)                  | Guangdong Zhongsheng Pharmaceutical Co. Ltd. (Dongguan City, China) | \$9.75    | Partnership to develop small interfering RNA for diabetic retinopathy and age-related macular degeneration  | The partnership will focus on clinical development and commercialization of STP60I; Guangdong will commit \$9.75M including up-front and milestone payments, and Sirnaomics also will be eligible for royalty sharing (6/24)     |
| <b>Unigene Laboratories Inc.</b> (Boonton, N.J.)           | China Pharmaceutical Group Ltd. (Hong Kong)                         | \$1.05    | Deal to sell its 45% equity interest in Chinese joint venture Unigene Biotechnology Co. Ltd. to China Pharmaceutical Group or one of its affiliates for \$1.05M                                     | All technology licenses, sub-licenses and other rights granted to the joint venture and China Pharmaceutical Group have been returned to Unigene; the venture was originally formed in June 2000 (6/14)                          |

| Company (Location)                                   | Company (Location)                             | Value (M) | Type/Product Area  | Terms/Details (Date)  |
|--|--|-----------|--|---|
| <b>Zealand Pharma A/S</b><br>(Copenhagen, Denmark)   | Boehringer Ingelheim GmbH (Ingelheim, Germany) | \$537.3   | Licensing agreement for exclusive global development and commercialization rights to its lead glucagon-GLP-1 dual agonist drug candidate, ZP2929 to treat Type II diabetes and obesity | Zealand could earn as much as \$537.3M in milestone and other payments, including \$57.76M during the first two years (6/17)  |
| <b>JULY</b>  |  |           |  |   |
| <b>Array BioPharma Inc.</b><br>(Boulder, Colo.)      | Aslan Pharmaceuticals Pte Ltd. (Singapore)     | ND        | License agreement to develop Array's HER2/EGFR inhibitor, ARRY-543, currently starting Phase II development for solid tumors   | Aslan will fund and develop it through proof of concept, initially targeting patients with gastric cancer through a program conducted in Asia; if proof of concept is achieved, Aslan will identify a global partner for Phase III development and commercialization (7/14) |
| <b>Astellas Pharma Inc.</b><br>(Tokyo)               | Royalty Pharma (New York)                      | \$609     | Astellas sold its IP assets relating to Prosidion's dipeptidyl peptidase IV inhibitors for Type II diabetes  | Royalty Pharma paid \$609M and will now receive all royalty payments and milestones (7/5)   |
| <b>Cambrex Corp.</b> (East Rutherford, N.J.)         | Tillotts Pharma AG (Rheinfelden, Switzerland)  | ND        | Development and commercialization agreement for a mesalamine-based technology for use in the treatment of inflammatory bowel disease   | Tillotts acquired the worldwide exclusive rights to develop and commercialize products based on Cambrex' 5-ASA-based technology in exchange for undisclosed milestone payments, as well as royalties (7/7)  |
| <b>Innate Pharma SA</b><br>(Marseilles, France)      | Bristol-Myers Squibb Co. (Princeton, N.J.)     | \$465     | Collaboration for exclusive worldwide rights to IPH2102, as well as to related compounds designed to block KIR receptors, for all potential indications                                | Innate will receive \$35M up front, and BMS will fund work on IPH2102 and agreed to pay up to \$430M in development and commercialization milestones, plus tiered, double-digit royalties on worldwide net sales (7/7)  |
| <b>MediciNova Inc.</b> (San Diego)                   | Zhejiang Medicine Co. Ltd. (Hangzhou, China)   | ND        | Joint venture to develop and commercialize MediciNova's MN-221 in China  | The product is in development to treat acute exacerbations of asthma and chronic obstructive pulmonary disease (7/5)  |
| <b>MingSight Pharmaceuticals</b><br>(Taizhou, China) | Shenzen Relin Medicin (Shenzen, China)         | ND        | Joint venture to develop and commercialize a therapy for diabetic eye disease in China   | The new venture, MingSight-Relin, will advance MS-533 (7/7)   |

| Company (Location)  | Company (Location)                                 | Value (M) | Type/Product Area  | Terms/Details (Date)  |
|---|--|-----------|--|---|
| <b>Pharmasset Inc.</b><br>(Princeton, N.J.)                 | Tibotec<br>Pharmaceuticals Inc.<br>(Raritan, N.J.) | ND        | Collaboration to evaluate its nucleotide polymerase inhibitor PSI-7977 in combination with Tibotec's protease inhibitor TMC435 in a Phase II study in chronic hepatitis C virus                            | Financial terms were not disclosed (7/7)  |
| <b>Rib-X<br/>Pharmaceuticals Inc.</b><br>(New Haven, Conn.) | Sanofi SA (Paris)                                  | \$763     | Exclusive worldwide research collaboration and licensing option for antibiotics resulting from its RX-04 program to treat resistant Gram-positive and resistant Gram-negative pathogens                    | Rib-X will receive \$10M in an up-front payment and is eligible to receive up to an additional \$9M in near-term research-based milestones, plus up to \$86M in development and regulatory milestones, and more than \$100M for commercial milestones, for a minimum of four target product profiles; total milestones could reach \$744M (7/7) |
| <b>Vical Inc.</b> (San Diego)                               | Astellas Pharma Inc.<br>(Tokyo)                    | \$130     | License agreement for worldwide development and commercialization of Vical's TransVax vaccine for cytomegalovirus reactivation in hematopoietic stem cell transplant and solid organ transplant recipients | Vical will get \$25M up front and \$10M more when design of a Phase III trial is completed; milestone payments of \$95M could bring the total to \$130M through launch, and Vical also could receive double-digit royalties (7/18)  |

## 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 and pharmaceutical 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 And Pharmaceutical Companies: June 1 - July 22, 2011

| Company (Location)                                     | Company (Location)                                    | Value (M) | Type/Product Area   | Terms/Details (Date)   |
|--|---|-----------|---|--|
| <b>JUNE</b>  |   |           |   |  |
| <b>D-Pharm Ltd.</b> (Rehovot, Israel)                  | Jiangsu NHWA Pharmaceutical Co. Ltd. (China)          | ND        | Partnership to commercialize D-Pharm's DP-VPA therapy for Epilepsy in China   | D-Pharm will receive up-front and developmental milestone payments, plus sales bonuses and royalties (6/1)   |
| <b>Ligand Pharmaceuticals Inc.</b> (San Diego)         | Merck & Co. Inc. (Whitehouse Station, N.J.)           | ND        | Captisol supply agreement for an undisclosed program  | Ligand will supply clinical and commercial supplies of Captisol and, if the program is approved for commercialization, expects to deliver multiple metric tons annually (6/21)   |
| <b>Medivir AB</b> (Huddinge, Sweden)                   | Daewoong Pharmaceutical Co. Ltd. (Seoul, South Korea) | ND        | Agreement to distribute Xerclear, a cold sore treatment, in China and Hong Kong   | Daewoong will carry out clinical studies and obtain regulatory approval for marketing and sales of the product in those territories; Medivir will be eligible for royalties (6/24)   |
| <b>JULY</b>  |   |           |   |  |
| <b>Merck &amp; Co. Inc.</b> (Whitehouse Station, N.J.) | Roche AG (Basel, Switzerland)                         | ND        | Nonexclusive deal for the global promotion of protease inhibitor Victrelis as part of a triple combination therapy regimen with peginterferon alfa and ribavirin                  | The firms previously disclosed an agreement to promote Victrelis in the U.S., where it gained marketing approval this year (7/21)  |
| <b>Victory Pharma Inc.</b> (San Diego)                 | Shionogi Inc. (Florham Park, N.J.)                    | \$127     | Agreement for Shionogi to acquire all currently marketed products from Victory, including seven treatments for pain and two for infectious diseases                               | The FDA-approved products will be marketed by Shionogi's existing sales force; terms indicated a \$118M cash payment at closing with up to \$9M in additional milestone payments (7/19)  |
| <b>Wellstat Therapeutics Corp.</b> (Gaithersburg, Md.) | BTG International Inc. (London)                       | ND        | Deal for U.S. marketing rights for uridine triacetate to treat accidental overexposure to chemotherapy drug fluorouracil due to dosing errors or impaired clearance from the body | BTG gains rights in the U.S. for up to 10 years after approval, while Wellstat retains them outside the U.S. and for all other potential uses; Wellstat gets an up-front payment, milestone payments, transfer pricing payments based on manufacturing costs and a significant percentage of net sales (7/7) |

**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*.

This chart may include collaborations between two pharmaceutical companies that involve a biotech product.

## Biotech – Big Pharma Collaborations: Modified And Terminated Agreements, June 1 - July 22, 2011

| Company (Location)  | Company (Location)   | Value (M) | Type/Product Area   | Terms/Details (Date)   |
|---|--|-----------|---|--|
| <b>I. MODIFIED AGREEMENTS</b>                                 |  |           |   |  |
| <b>JUNE</b>   |  |           |   |  |
| <b>Dyax Corp.</b><br>(Cambridge, Mass.)                       | Defiante Farmaceutica SA<br>(affiliate of Sigma-Tau Group; Rome) | \$17      | Expanded partnership for Kalbitor to treat hereditary angioedema and other indications to include development and commercialization rights in Latin America, excluding Mexico, and the Caribbean, Taiwan, Singapore and South Korea | Dyax will receive an up-front payment of \$7M and is eligible to receive as much as \$10M in milestones (6/1)  |
| <b>pSivida Corp.</b><br>(Watertown, Mass.)                    | Pfizer Inc. (New York)   | \$2.3     | Amended agreement to focus solely on a sustained-release implant for ocular hypertension and glaucoma   | The product will deliver latanoprost using a system based on pSivida's Durasert technology; Pfizer will pay \$2.3M initially, and pSivida will develop it through Phase II trials; at that point, Pfizer can exercise an option for \$20M to develop and commercialize the product globally; pSivida would be eligible for milestone payments worth up to \$146.5M, plus double-digit royalties (6/16) |
| <b>JULY</b>   |  |           |   |  |
| <b>Cel-Sci Corp.</b> (Vienna, Va.)                            | Teva Pharmaceutical Industries Ltd. (Jerusalem)                  | ND        | Expanded licensing agreement for marketing rights to Phase III-stage head and neck cancer drug Multikine to include Croatia and Serbia  | The original deal gave Teva rights in Israel and Turkey; Cel-Sci is entitled to milestone payments upon approval, and the firms will share revenue generated from all four countries (7/20)  |
| <b>Cyclacel Pharmaceuticals Inc.</b> (Berkeley Heights, N.J.) | Daiichi Sankyo Co. Ltd. (Tokyo)                                  | ND        | Amended licensing deal with Daiichi irrevocably waiving a termination right under the original deal that required the company to obtain regulatory approval for selling sapacitabine in at least one country by September           | The amendment also increases Cyclacel's royalty from Daiichi on future net sales by a percentage between 1.25% and 1.5%, depending on the level of net sales realized (7/19)   |

| Company (Location)                                | Company (Location)   | Value (M) | Type/Product Area   | Terms/Details (Date)  |
|---|--|-----------|---|---|
| <b>Gilead Sciences Inc.</b> (Foster City, Calif.) | Hetero Drugs Ltd., Matrix Laboratories Ltd., Ranbaxy Laboratories Ltd. and Strides Arcolab Ltd. (all of India) | ND        | New licensing terms for three HIV/AIDS drugs currently in late-stage clinical development | The terms grant the Medicines Patent Pool Foundation and Gilead's Indian partners future rights to elvitegravir, an integrase inhibitor; cobicistat, an antiretroviral boosting agent; and the "Quad," which combines four Gilead HIV medicines in a once-daily, single-tablet regimen (7/13) |

## I. TERMINATED AGREEMENTS

### JUNE

|  |   |        |  |  |
|--|---|--------|--|--|
| <b>Adolor Corp.</b> (Exton, Pa.)                         | GlaxoSmithKline plc (London)  | ND     | Terminated deal for constipation drug Entereg  | Adolor regains all rights three years after restrictive labeling and labor-intensive postmarketing requirements crushed hopes for a potential blockbuster (6/16)   |
| <b>Diamyd AB</b> (Stockholm, Sweden)                     | Ortho-McNeil-Janssen Pharmaceuticals (subsidiary of Johnson & Johnson; New Brunswick, N.J.) | \$45   | Terminated deal for license rights to diabetes therapy Diamyd  | The decision to terminate came following disappointing data from a Phase III trial showing Diamyd failed to meet its primary endpoint in Type I diabetes; Diamyd received a nonrefundable \$45M payment when the deal was signed (6/2) |
| <b>NovaBay Pharmaceuticals Inc.</b> (Emeryville, Calif.) | Alcon Inc. (Huenenberg, Switzerland)  | \$2.97 | Terminated deal for worldwide rights to NovaBay's topical Aganocide compounds for antibiotic-resistant eye, ear and sinus infections | NovaBay is receiving a \$2.97M termination payment (6/17)  |

### JULY

|  |                                     |       |   |  |
|--|-------------------------------------|-------|---|--|
| <b>Exelixis Inc.</b> (South San Francisco)           | Bristol-Myers Squibb Co. (New York) | \$465 | Terminated deal for XL281, a RAF kinase inhibitor against solid tumors  | Exelixis was eligible for development and regulatory milestones of up to \$315M and sales milestones of up to \$150M for XL281; the company said it has no intention of advancing the compound (7/18)                          |
| <b>Idera Pharmaceuticals Inc.</b> (Cambridge, Mass.) | Merck KGaA (Darmstadt, Germany)     | \$418 | Merck backed off from development of IMO-2055, a TLR9 agonist, based on an increased incidence of neutropenia and electrolyte imbalances in head and neck cancer patients | Merck will continue developing follow-on compounds covered by the 2007 license and collaboration agreement; Idera has received \$52M already and could see up to \$366M in additional milestone payments, plus royalties (7/8) |

#### Notes:

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

## The Week's Biggest Gainers and Losers

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

| (By Percent)      | (By Dollars) | (By Percent)        | (By Dollars) |
|-------------------|--------------|---------------------|--------------|
| MDRNA             | 25.00        | Pharmasset          | 11.43        |
| Oncothyreon       | 19.63        | Alexion Pharma      | 6.61         |
| Access Pharma     | 19.02        | Pharma Prdt Dev     | 2.84         |
| Labopharm         | 18.75        | Gilead Sciences     | 2.21         |
| Avanir            | 15.04        | Regeneron Pharma    | 1.88         |
| Catalyst Pharma   | 13.33        | Oncothyreon         | 1.59         |
| Vical             | 12.80        | Biogen Idec         | 1.56         |
| Alexion Pharma    | 12.62        | Pacific Biosciences | 1.03         |
| Pharma Prdt Dev   | 10.19        | BioMarin Pharma     | 1.02         |
| Cell Therapeutics | 9.35         | Amylin Pharma       | 0.82         |

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

| (By Percent)       | (By Dollars) | (By Percent)     | (By Dollars) |
|--------------------|--------------|------------------|--------------|
| Nabi Biopharma     | -63.23       | Nabi Biopharma   | -3.56        |
| Cortex Pharma      | -20.00       | AMAG Pharma      | -2.42        |
| Alseres            | -20.00       | 3S Bio           | -1.72        |
| Pharmos            | -16.67       | Human Genome     | -1.7         |
| Dynavax            | -15.56       | Ventrus Biosci   | -1.07        |
| StemCells          | -14.63       | Seattle Genetics | -0.96        |
| AMAG Pharma        | -13.25       | Targacept        | -0.9         |
| Progenics Pharma   | -10.85       | Progenics Pharma | -0.8         |
| Allos Therapeutics | -10.00       | Alkermes         | -0.7         |
| Bio-path Holdings  | -10.00       | StemCells        | -0.66        |

## BioWorld Stock Report For Public Biotechnology Companies

| Company            | Symbol | Close 7/15 | Close 7/22 | %Change WK | %Change YTD | Vol (000) |
|--------------------|--------|------------|------------|------------|-------------|-----------|
| 3S Bio             | SSRX   | 17.96      | 16.24      | -9.58      | 8.41        | 216       |
| Aastrom Biosci     | ASTM   | 2.65       | 2.85       | 7.55       | 11.33       | 2119      |
| Acadia Pharma      | ACAD   | 1.7        | 1.67       | -1.76      | 35.77       | 573       |
| Accentia Biopharma | ABPI   | 0.45       | 0.44       | -2.22      | -41.33      | 64        |
| Access Pharma      | ACCP   | 2.05       | 2.44       | 19.02      | -0.41       | 320       |
| AcelRx Pharma      | ACRX   | 4.42       | 4.38       | -0.90      | -3.74       | 59        |
| Achillion          | ACHN   | 7.49       | 7.64       | 2.00       | 88.18       | 3335      |
| Acorda Therap      | ACOR   | 29.63      | 29.67      | 0.13       | 7.85        | 2439      |
| Adamis             | ADMP   | 0.22       | 0.24       | 9.09       | 17.07       | 603       |
| Adolor             | ADLR   | 2.43       | 2.48       | 2.06       | 100.00      | 1949      |
| Aegerion Pharma    | AEGR   | 15.22      | 15.6       | 2.50       | 10.09       | 173       |
| AEterna Zentaris   | AEZS   | 2.31       | 2.25       | -2.60      | 28.57       | 4522      |
| Affymax            | AFFY   | 7.43       | 7.25       | -2.42      | 9.02        | 1791      |
| Agenus             | AGEN   | 0.77       | 0.81       | 5.19       | -19.80      | 721       |
| Albany Molecular   | AMRI   | 4.84       | 4.83       | -0.21      | -17.86      | 226       |
| Alexion Pharma     | ALXN   | 52.37      | 58.98      | 12.62      | -26.87      | 9947      |
| Alexza Pharma      | ALXA   | 1.7        | 1.78       | 4.71       | 41.27       | 2228      |
| Alimera Sciences   | ALIM   | 8.76       | 8.97       | 2.40       | -12.14      | 308       |
| Alkermes           | ALKS   | 19.27      | 18.57      | -3.63      | 50.98       | 4452      |
| Allos Therapeutics | ALTH   | 2          | 1.8        | -10.00     | -61.04      | 33891     |
| Alnylam Pharma     | ALNY   | 10.26      | 9.89       | -3.61      | 0.10        | 711       |
| Alseres            | ALSE   | 0.1        | 0.08       | -20.00     | -38.46      | 18        |
| AMAG Pharma        | AMAG   | 18.27      | 15.85      | -13.25     | -12.77      | 2997      |
| Amarin             | AMRN   | 13.63      | 14.45      | 6.02       | 74.31       | 9473      |
| Amgen              | AMGN   | 55.05      | 55.22      | 0.31       | -0.56       | 23823     |
| Amicus             | FOLD   | 7.5        | 7.25       | -3.33      | 51.36       | 267       |
| Ampliphi Biosci    | APHB   | 0.24       | 0.23       | -4.17      | -8.00       | 152       |
| Amylin Pharma      | AMLN   | 12.83      | 13.65      | 6.39       | -8.33       | 8851      |
| Anacor Pharma      | ANAC   | 6.46       | 6.47       | 0.15       | 20.48       | 87        |
| Anthera Pharma     | ANTH   | 8.01       | 8.1        | 1.12       | 66.32       | 180       |
| Ardea Biosciences  | RDEA   | 24.73      | 24.85      | 0.49       | -5.44       | 345       |
| Arena Pharma       | ARNA   | 1.44       | 1.57       | 9.03       | -8.19       | 8029      |
| Ariad Pharma       | ARIA   | 12.58      | 13.34      | 6.04       | 157.53      | 15856     |
| ArQule             | ARQL   | 6.33       | 6.44       | 1.74       | 11.23       | 627       |
| Array BioPharma    | ARRY   | 2.5        | 2.41       | -3.60      | -19.13      | 823       |
| Aryx               | ARYX   | 0.03       | 0.03       | 0.00       | -88.89      | 181       |
| Auxilium Pharma    | AUXL   | 20.37      | 20.08      | -1.42      | -5.33       | 2845      |
| Avanir             | AVNR   | 3.39       | 3.9        | 15.04      | -2.74       | 10088     |
| Avax Tech          | AVXT   | 0.03       | 0.03       | 0.00       | -33.33      | 73        |
| AVEO Pharma        | AVEO   | 20.03      | 19.62      | -2.05      | 33.47       | 1317      |
| AVI BioPharma      | AVII   | 1.61       | 1.6        | -0.62      | -25.93      | 4736      |
| Bellus Health      | BLUS   | 0.06       | 0.06       | 0.00       | -61.29      | 249       |
| BG Medicine        | BGMD   | 8.33       | 8.08       | -3.00      | -2.65       | 28        |
| BioCryst Pharma    | BCRX   | 3.93       | 3.89       | -1.02      | -24.17      | 540       |
| Biodel             | BIOD   | 2.01       | 1.96       | -2.49      | 2.08        | 821       |
| Biodelivery Sci    | BDSI   | 3.62       | 3.91       | 8.01       | 5.68        | 798       |
| Biogen Idec        | BIIB   | 104        | 105.56     | 1.50       | 58.02       | 6669      |
| BioMarin Pharma    | BMRN   | 29.69      | 30.71      | 3.44       | 13.03       | 4340      |
| Bio-path Holdings  | BPTH   | 0.3        | 0.27       | -10.00     | -25.00      | 42        |
| BioSante Pharma    | BPAX   | 3.64       | 3.58       | -1.65      | 115.66      | 8484      |
| Cadence Pharma     | CADX   | 8.62       | 8.55       | -0.81      | 13.40       | 2006      |
| Cardiome           | CRME   | 4.23       | 4.35       | 2.84       | -33.59      | 1057      |
| Cardiovascular Bio | CVBT   | 0.32       | 0.29       | -9.38      | -14.71      | 684       |
| Catalyst Pharma    | CPRX   | 1.5        | 1.7        | 13.33      | 77.08       | 265       |
| Celgene            | CELG   | 60.67      | 61.18      | 0.84       | 2.94        | 12991     |

| Company            | Symbol | Close 7/15 | Close 7/22 | %Change WK | %Change YTD | Vol (000) |
|--------------------|--------|------------|------------|------------|-------------|-----------|
| Cell Therapeutics  | CTIC   | 1.39       | 1.52       | 9.35       | 308.60      | 8158      |
| Celldex Therap     | CLDX   | 3.71       | 3.65       | -1.62      | -12.47      | 1292      |
| CEL-SCI            | CVM    | 0.5        | 0.5        | 0.00       | -39.93      | 4473      |
| Cephalon           | CEPH   | 79.99      | 80.21      | 0.28       | 29.04       | 6686      |
| Cerus              | CERS   | 2.86       | 2.94       | 2.80       | 18.55       | 853       |
| Chelsea Therap     | CHTP   | 5.89       | 5.31       | -9.85      | -30.04      | 2330      |
| Cleveland Biolabs  | CBLI   | 3.13       | 3.15       | 0.64       | -56.19      | 1193      |
| Codexis            | CDXS   | 9.26       | 9.25       | -0.11      | -12.74      | 345       |
| Columbia Labs      | CBRX   | 3.19       | 3.22       | 0.94       | 47.03       | 1931      |
| CombiMatrix        | CBMX   | 3.33       | 3.39       | 1.80       | 52.02       | 28        |
| Complete Genomics  | GNOM   | 14.7       | 14.36      | -2.31      | 92.24       | 881       |
| Compugen           | CGEN   | 4.02       | 4.07       | 1.24       | -18.27      | 190       |
| Corcept            | CORT   | 3.81       | 3.89       | 2.10       | -0.77       | 814       |
| CorMedix           | CRMD   | 1.45       | 1.35       | -6.90      | -23.30      | 66        |
| Cornerstone Therap | CRTX   | 8.6        | 8.18       | -4.88      | 44.78       | 117       |
| Cortex Pharma      | CORX   | 0.1        | 0.08       | -20.00     | -55.56      | 237       |
| Cubist Pharma      | CBST   | 35.9       | 35.72      | -0.50      | 65.52       | 4146      |
| Curis              | CRIS   | 3.99       | 4.23       | 6.02       | 109.41      | 2301      |
| Cytokinetics       | CYTK   | 1.3        | 1.29       | -0.77      | -38.28      | 1494      |
| CytRx              | CYTR   | 0.73       | 0.71       | -2.74      | -29.00      | 1932      |
| Dara Biosciences   | DARA   | 2.55       | 2.46       | -3.53      | -27.00      | 71        |
| Dendreon           | DNDN   | 38.8       | 39.1       | 0.77       | 10.42       | 7555      |
| DepoMed            | DEPO   | 8.31       | 8.54       | 2.77       | 31.79       | 2761      |
| DiaDexus           | DDXS   | 0.32       | 0.32       | 0.00       | 10.34       | 134       |
| Discovery Labs     | DSCO   | 2.59       | 2.54       | -1.93      | -23.72      | 1403      |
| DURECT             | DRRX   | 2.11       | 2.2        | 4.27       | -38.03      | 1478      |
| Dusa Pharma        | DUSA   | 5.54       | 5.47       | -1.26      | 122.36      | 1038      |
| Dyax               | DYAX   | 2.03       | 1.87       | -7.88      | -10.53      | 6005      |
| Dynavax            | DVAX   | 3.02       | 2.55       | -15.56     | -17.74      | 27562     |
| Emergent BioSol    | EBS    | 21.76      | 21.47      | -1.33      | -9.33       | 745       |
| Emisphere Tech     | EMIS   | 0.92       | 0.95       | 3.26       | -59.92      | 201       |
| Endocyte           | ECYT   | 12.01      | 11.43      | -4.83      | 47.87       | 1089      |
| Entremed           | ENMD   | 2.05       | 1.97       | -3.90      | -61.22      | 341       |
| Enzo Biochem       | ENZ    | 4.28       | 4.05       | -5.37      | -25.41      | 653       |
| Enzon Pharma       | ENZN   | 10.26      | 10.25      | -0.10      | -15.98      | 1230      |
| Epicept            | EPCT   | 0.54       | 0.51       | -5.56      | -40.00      | 31        |
| Exelixis           | EXEL   | 8.89       | 8.68       | -2.36      | 1.05        | 2700      |
| Flamel Tech        | FLML   | 5.13       | 5.15       | 0.39       | -26.01      | 54        |
| Forest Labs        | FRX    | 38.46      | 38.53      | 0.18       | 20.52       | 14360     |
| Furiex Pharma      | FURX   | 18.01      | 17.64      | -2.05      | 22.08       |           |
| Genexx Biotech     | GNBT   | 0.14       | 0.14       | 0.00       | -52.53      | 5772      |
| Genomic Health     | GHDX   | 27.37      | 28.1       | 2.67       | 28.43       | 283       |
| GenVec             | GNVC   | 3.14       | 3.07       | -2.23      | 438.60      | 816       |
| Geron              | GERN   | 4.03       | 4.16       | 3.23       | -20.15      | 6635      |
| Gilead Sciences    | GILD   | 41         | 43.21      | 5.39       | 19.17       | 34824     |
| GTx                | GTXI   | 4.66       | 4.79       | 2.79       | 73.55       | 2281      |
| Harbor Biosci      | HRBR   | 0.2        | 0.19       | -5.00      | 46.15       | 214       |
| Harvard Bio        | HBIO   | 5.66       | 5.7        | 0.71       | 40.39       | 387       |
| Human Genome       | HGSI   | 23.2       | 21.5       | -7.33      | -11.16      | 24719     |
| Idenix Pharma      | IDIX   | 6.08       | 6.34       | 4.28       | 27.05       | 2947      |
| Idera Pharma       | IDRA   | 1.93       | 1.85       | -4.15      | -36.21      | 81        |
| ImmunoGen          | IMGN   | 15.4       | 15.2       | -1.30      | 61.36       | 4130      |
| Immunomedics       | IMMU   | 4.13       | 4.3        | 4.12       | 19.44       | 1955      |
| Incyte             | INCY   | 20.07      | 19.63      | -2.19      | 17.05       | 3669      |
| Infinity Pharma    | INFI   | 9.16       | 9.96       | 8.73       | 64.63       | 600       |

| Company             | Symbol | Close 7/15 | Close 7/22 | %Change WK | %Change YTD | Vol (000) |
|---------------------|--------|------------|------------|------------|-------------|-----------|
| Inhibitex           | INHX   | 3.99       | 4.27       | 7.02       | 58.74       | 1341      |
| InterMune           | ITMN   | 37.01      | 37.02      | 0.03       | 0.30        | 2361      |
| Ironwood Pharma     | IRWD   | 15.79      | 15.3       | -3.10      | 47.83       | 708       |
| ISIS Pharma         | ISIS   | 9.12       | 8.79       | -3.62      | -13.40      | 2646      |
| Keryx Biopharma     | KERX   | 4.91       | 4.74       | -3.46      | 1.50        | 4029      |
| Labopharm           | DDSSF  | 0.16       | 0.19       | 18.75      | -80.00      | 82        |
| Lexicon             | LXRX   | 1.75       | 1.78       | 1.71       | 19.46       | 3193      |
| Ligand Pharma       | LGND   | 11.55      | 12.36      | 7.01       | 38.72       | 348       |
| MannKind            | MNKD   | 3.66       | 3.55       | -3.01      | -56.33      | 2573      |
| Map Pharma          | MAPP   | 16.04      | 16.3       | 1.62       | -2.16       | 442       |
| Maxygen             | MAXY   | 5.47       | 5.47       | 0.00       | 38.83       | 669       |
| MDRNA               | MRNA   | 0.2        | 0.25       | 25.00      | -83.65      | 15248     |
| Metabolix Inc.      | MBLX   | 6.81       | 6.69       | -1.76      | -43.78      | 1144      |
| Micromet            | MITI   | 6.29       | 6.08       | -3.34      | -26.48      | 2698      |
| Momenta Pharma      | MNTA   | 19.51      | 19.4       | -0.56      | 29.16       | 3640      |
| Myrexia             | MYRX   | 3.56       | 3.47       | -2.53      | -18.35      | 415       |
| Myriad Genetics     | MYGN   | 23.56      | 23.33      | -0.98      | 1.74        | 2380      |
| Nabi Biopharma      | NABI   | 5.63       | 2.07       | -63.23     | -64.62      | 29620     |
| Nanogen             | NGEN   | 0.01       | 0.01       | 0.00       | 17.65       | 20        |
| Nektar Therap       | NKTR   | 7.65       | 7.36       | -3.79      | -43.21      | 3232      |
| Neurocrine Biosci   | NBIX   | 8.02       | 8.27       | 3.12       | 7.54        | 971       |
| NeurogesX           | NGSX   | 1.7        | 1.67       | -1.76      | -73.58      | 519       |
| NovaBay             | NBY    | 1.05       | 1.02       | -2.86      | -38.92      | 210       |
| Novavax             | NVAX   | 1.96       | 2.13       | 8.67       | -16.47      | 2290      |
| NPS Pharma          | NPSP   | 9.91       | 9.66       | -2.52      | 20.45       | 2349      |
| NuPathe             | PATH   | 7.29       | 7.06       | -3.16      | -22.08      | 382       |
| Omeros              | OMER   | 4.14       | 4.16       | 0.48       | -50.24      | 171       |
| OncoGenex Pharma    | OGXI   | 15.83      | 15.7       | -0.82      | -4.56       | 103       |
| Oncothyreon         | ONTY   | 8.1        | 9.69       | 19.63      | 196.33      | 19144     |
| Onyx Pharma         | ONXX   | 34.66      | 34.52      | -0.40      | -6.58       | 2595      |
| Opko Health         | OPK    | 4.3        | 4.4        | 2.33       | 18.60       | 6137      |
| Optimer Pharma      | OPTR   | 11.42      | 11.08      | -2.98      | -3.65       | 2083      |
| OraSure Tech        | OSUR   | 9.82       | 9.77       | -0.51      | 63.65       | 789       |
| Orexigen            | OREX   | 1.68       | 1.69       | 0.60       | -79.29      | 1538      |
| Osiris Thera        | OSIR   | 7.95       | 7.8        | -1.89      | -1.76       | 316       |
| Oxis International  | OXIS   | 0.08       | 0.08       | 0.00       | -40.74      | 118       |
| Pacific Biosciences | PACB   | 11.09      | 12.12      | 9.29       | -23.82      | 815       |
| Pacira Pharma       | PCRX   | 11.46      | 11.81      | 3.05       | 68.23       | 424       |
| Pain Therapeutics   | PTIE   | 4.61       | 4.97       | 7.81       | -25.71      | 1677      |
| Palatin Tech        | PTN    | 1.05       | 1.11       | 5.71       | -13.95      | 1494      |
| Panacos Pharma      | PANC   | 0.01       | 0.01       | 0.00       | 0.00        | 45        |
| Peregrine Pharma    | PPHM   | 1.88       | 1.81       | -3.72      | -17.73      | 1443      |
| Pharma Prdt Dev     | PPDI   | 27.86      | 30.7       | 10.19      | 11.60       | 13043     |
| Pharmacycyclics     | PCYC   | 12.13      | 12.75      | 5.11       | 104.33      | 2913      |
| Pharmasset          | VRUS   | 125.54     | 136.97     | 9.10       | 211.72      | 2641      |
| Pharmos             | PARS   | 0.12       | 0.1        | -16.67     | 0.00        | 26        |
| Poniard Pharma      | PARD   | 0.21       | 0.21       | 0.00       | -63.79      | 261       |
| Pozen               | POZN   | 4.58       | 4.81       | 5.02       | -26.79      | 683       |
| Progenics Pharma    | PGNX   | 7.37       | 6.57       | -10.85     | 21.44       | 593       |
| Protalix Biothera   | PLX    | 6.79       | 6.75       | -0.59      | -32.36      | 1935      |
| Protein Design      | PDLI   | 6.26       | 6.35       | 1.44       | 2.09        | 9004      |
| Qiagen              | QGEN   | 18.28      | 17.88      | -2.19      | -8.07       | 6195      |
| QLT Inc.            | QLTI   | 7.09       | 6.77       | -4.51      | -5.45       | 553       |
| Raptor Pharma       | RPTP   | 6.54       | 6.96       | 6.42       | 91.21       | 2665      |
| Regeneron Pharma    | REGN   | 55.59      | 57.47      | 3.38       | 72.17       | 3460      |
| Repligen            | RGEN   | 3.71       | 3.7        | -0.27      | -21.73      | 141       |
| Rexahn Pharma       | RNN    | 1.26       | 1.27       | 0.79       | 10.43       | 1722      |
| Rigel Pharma        | RIGL   | 10.15      | 9.88       | -2.66      | 30.00       | 2587      |
| Rosetta Genomics    | ROSGD  | 1.54       | 1.47       | -4.55      | 54.74       | 305       |
| Rxi Pharma          | RXII   | 1.28       | 1.29       | 0.78       | -51.14      | 3665      |
| Sagent Pharma       | SGNT   | 23.97      | 23.62      | -1.46      | 23.08       | 261       |
| Sangamo Biosci      | SGMO   | 5.98       | 6.16       | 3.01       | -10.20      | 1618      |
| Santarus            | SNTS   | 3.27       | 3.35       | 2.45       | 1.82        | 657       |
| Savient Pharma      | SVNT   | 7.72       | 7.85       | 1.68       | -30.10      | 3966      |
| SciClone Pharma     | SCLN   | 6.41       | 6.75       | 5.30       | 59.20       | 1888      |
| Seattle Genetics    | SGEN   | 18.87      | 17.91      | -5.09      | 16.75       | 10827     |
| Sequenom            | SQNM   | 7.55       | 7.73       | 2.38       | -5.04       | 4363      |
| SIGA Tech           | SIGA   | 8.8        | 8.23       | -6.48      | -41.05      | 2684      |
| Somaxon Pharma      | SOMX   | 1.6        | 1.73       | 8.12       | -46.11      | 2615      |
| Spectrum Pharma     | SPPI   | 10.63      | 11.23      | 5.64       | 58.62       | 7268      |
| StemCells           | STEMD  | 4.51       | 3.85       | -14.63     | 246.85      | 793       |
| Sucampo Pharma      | SCMP   | 4.13       | 4.15       | 0.48       | 8.36        | 65        |
| SuperGen            | SUPG   | 3.01       | 3.14       | 4.32       | 18.94       | 1783      |
| Synta Pharma        | SNTA   | 4.95       | 4.87       | -1.62      | -20.42      | 675       |
| Talon Thera         | TLON   | 1          | 0.96       | -4.00      | 100.00      | 426       |
| Targacept           | TRGT   | 21.95      | 21.05      | -4.10      | -21.13      | 698       |
| Telik               | TELK   | 0.64       | 0.58       | -9.38      | -27.95      | 235       |
| Tengion             | TNGN   | 1.33       | 1.38       | 3.76       | -49.64      | 192       |
| Theravance          | THRX   | 24.18      | 24.8       | 2.56       | -2.94       | 1002      |
| Titan Pharma        | TTNP   | 1.95       | 1.92       | -1.54      | 57.38       | 567       |
| Transcept Pharma    | TSPT   | 4.87       | 4.4        | -9.65      | -41.72      | 1515      |

| Company             | Symbol | Close 7/15 | Close 7/22 | %Change WK | %Change YTD | Vol (000) |
|---------------------|--------|------------|------------|------------|-------------|-----------|
| Transgenomic        | TBIO   | 1.65       | 1.53       | -7.27      | 115.49      | 272       |
| Tranzyme            | TZYM   | 4.12       | 4.25       | 3.16       | 6.25        | 23        |
| Trimeris            | TRMS   | 2.52       | 2.53       | 0.40       | 3.69        | 2472      |
| Trinity Biotech     | TRIB   | 10.06      | 10.72      | 6.56       | 21.27       | 342       |
| Trius Therap        | TSRX   | 7.82       | 7.95       | 1.66       | 119.92      | 171       |
| Unigene             | UGNE   | 1.2        | 1.1        | -8.33      | 64.18       | 287       |
| United Therap       | UTHR   | 56.22      | 56.68      | 0.82       | -10.50      | 3593      |
| Vanda Pharma        | VNDA   | 7.15       | 7.27       | 1.68       | -22.49      | 431       |
| Ventrus Biosciences | VTUS   | 12.96      | 11.89      | -8.26      | 79.61       | 587       |
| Vermillion          | VRML   | 3.94       | 4.07       | 3.30       | -45.15      | 899       |
| Vertex Pharma       | VRTX   | 50.68      | 50.98      | 0.59       | 44.26       | 5729      |
| Vical               | VICL   | 4.61       | 5.2        | 12.80      | 153.66      | 6348      |
| ViroPharma          | VPHM   | 19.34      | 19.71      | 1.91       | 11.99       | 1841      |
| Vivus               | VVUS   | 8.34       | 8.23       | -1.32      | -13.64      | 4666      |
| XenoPort            | XNPT   | 7.48       | 7.61       | 1.74       | -12.12      | 1131      |
| Zalucus Inc         | ZLCS   | 2.61       | 2.56       | -1.92      | 57.06       | 3810      |
| Zogenix             | ZGNX   | 5.03       | 4.97       | -1.19      | -12.35      | 265       |

**LONDON STOCK EXCHANGE**

| Company          | Symbol | 7/15  | 7/22  | %WK   | %YTD   | Volume |
|------------------|--------|-------|-------|-------|--------|--------|
| Antisoma         | ASM    | 2.47  | 2.4   | -2.83 | -92.73 | 7985   |
| Ark Therapeutics | AKT    | 4.925 | 5.025 | 2.03  | -64.23 | 1043   |
| Asterand         | ATD    | 10.10 | 4.375 | 4.38  | -43.88 | 503    |
| Oxford Biomedica | OXB    | 6.96  | 7.12  | 2.30  | -36.71 | 7047   |
| Phytopharm       | PYM    | 7.6   | 8.5   | 11.84 | -21.59 | 1576   |
| Puricore         | PURI   | 36.5  | 41.3  | 13.15 | 208.21 | 38     |
| Renovo Group     | RNVO   | 14.25 | 14.5  | 1.75  | -49.83 | 2936   |
| SkyePharma       | SKP    | 43    | 43.31 | 0.72  | -49.62 | 51     |
| Vernalis plc     | VER    | 39.5  | 44.25 | 12.03 | -49.14 | 337    |

Note: Prices are denoted in pence.

**TORONTO STOCK EXCHANGE**

| Company            | Symbol | 7/15 | 7/22 | %WK    | %YTD   | Volume |
|--------------------|--------|------|------|--------|--------|--------|
| Adherex Technol    | AHX    | 0.04 | 0.04 | 0.00   | -11.11 | 90     |
| Allon Therapeutics | NPC    | 0.36 | 0.4  | 11.11  | 25.00  | 256    |
| BELLUS Health      | BLU    | 0.06 | 0.06 | 0.00   | -66.67 | 6200   |
| Bioniche Life Sci  | BNC    | 0.9  | 0.87 | -3.33  | 55.36  | 413    |
| Cangene            | CNJ    | 1.57 | 1.69 | 7.64   | -66.86 | 103    |
| Isoteknika         | ISA    | 0.14 | 0.14 | 0.00   | -15.15 | 328    |
| Lorus Therap       | LOR    | 0.44 | 0.42 | -4.55  | 546.15 | 134    |
| Medicago           | MDG    | 0.47 | 0.47 | 0.00   | -29.85 | 0      |
| MethylGene         | MYG    | 0.35 | 0.3  | -14.29 | 7.14   | 256    |
| Oncolytics Biotech | ONC    | 4.61 | 4.34 | -5.86  | 57.82  | 631    |
| Protox Therap      | PRX    | 0.54 | 0.51 | -5.56  | -40.00 | 131    |
| Resverlogix        | RVX    | 1.48 | 1.41 | -4.73  | -41.74 | 214    |
| SemBioSys Gen      | SBS    | 0.07 | 0.08 | 14.29  | -60.00 | 61     |
| Tekmira Pharma     | TKM    | 2.25 | 2.47 | 9.78   | 165.59 | 42     |
| Thallion Pharma    | TLN    | 0.15 | 0.15 | 0.00   | 36.36  | 116    |
| Theratechnologies  | TH     | 4.22 | 4.19 | -0.71  | -5.42  | 333    |
| Wex Pharma         | WXI    | 0.15 | 0.15 | 0.00   | -9.09  | 0      |
| YM BioSciences     | YM     | 2.65 | 2.56 | -3.40  | 76.55  | 64     |

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: +0.28%**

Range: -63.23% to +25.00%; Number Of Companies: 209 (does not include LSE or TSX; not market weighted)

**Average Percent Change YTD: +12.61%**

Range: -88.89% to +438.60%; Number Of Companies: 209 (does not include LSE or TSX; not market weighted)

*Coronado Case Study***Form 10 Offers Alternative to IPO, Reverse Merger Listing****By Trista Morrison  
Editor**

Between poor pricings for initial public offerings (IPO) and investors (not to mention Nasdaq) cracking down on reverse mergers, it's not easy for private biotechs to get public these days. But a few companies are exploring an alternate route to public listing: the Form-10 pathway.

"This process is one that is arising out of the limitations and drawbacks with traditional methods," explained Fran Stoller, a partner with law firm Loeb & Loeb LLP. The firm advised Coronado Biosciences Inc. on its Form-10 filing last week. (See *BioWorld Today*, July 20, 2011.)

Although not many biotechs have pursued the Form-10 pathway yet, "we are talking to a number of private companies who are thinking about it," reported Annette Grimaldi, managing director with BMO Capital Markets Corp. She added that biotechs "tend to be early adopters of unusual strategies for going public" because they are often seeking to access the public markets while still unprofitable.

In essence, the Form-10 pathway creates a two-step process for going public. First, the company files a Form 10 with the SEC, which involves providing disclosures and financial statements similar to those required for an IPO. Once the SEC has reviewed and blessed the filing, the firm becomes a public reporting company.

Form-10 filings are required for private companies with 500 or more stockholders of record – something not often seen in biotech, where the majority of private firms are closely held by a small group of venture capitalists. But a company with less than 500 stockholders could choose to file a Form-10 and become a public reporting company. Once it did so, it would be qualified to embark on Step 2: filing an S-1 to register its shares and applying to list those shares on an exchange.

In the past, some Form-10 shell companies have been created solely for the purpose of serving as a vehicle to take another private firm public. A private biotech, for example, would then reverse-merge with the Form-10 shell. The trick, however, is that the merged entity would likely have to trade on the Pink Sheets or OTC Bulletin Board until it could qualify to transfer to a more mainstream exchange like the AMEX or Nasdaq, and Nasdaq has recently moved to make that transfer a lot harder for companies formed through reverse mergers. (See *story this issue*.)

Hence, Coronado skipped the reverse merger and filed its own Form 10. The biotech plans to list initially on the OTCBB, but hopes to transfer to AMEX or Nasdaq before the end of this year.

Unlike an IPO, the Form-10 pathway does not involve a process in which institutional investors help set the initial stock price. That might not be a bad thing: a recent *BioWorld Today* analysis showed biotech IPOs in 2011 priced 59.6 percent below their initial targets, on average. But with the Form-10 filer's stock price completely at the mercy of whatever buyers and sellers agree is fair, trading is likely to be erratic at first, Grimaldi said.

Also unlike an IPO, the Form-10 pathway does not involve investment bankers trotting management around to meet with institutional investors, raising awareness and creating a shareholder base. Thus, like firms that go public on a foreign exchange and then transfer to the OTCBB, or those that reverse merge into an OTCBB-listed firm, trading volume can be pretty low at the start. (See *BioWorld Insight*, March 21, 2011.)

And while an IPO usually involves the issuance of new shares in a financing, the Form-10 pathway does not. The

*See Form 10, page 5*

*"This process is one that is arising out of the limitations and drawbacks with traditional methods."*

– Fran Stoller, partner, Loeb & Loeb LLP

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## WEEK IN REVIEW

### Financings

**Celsion Corp.** raised \$13 million in a registered direct offering and \$5.4 million in a private placement.

**Coronado Biosciences Inc.** filed a Form-10 with the SEC as a non-IPO route to public listing.

**glCare Pharma Inc.** raised \$7 million in Series A financing to develop a colonic analgesic.

**NeoStem Inc.** is raising about \$16.5 million in a public offering of stock and warrants.

**Protox Therapeutics Inc.** entered a \$15 million loan agreement with Oxford Finance LLC.

**SARcode Bioscience Inc.** raised \$44 million in a Series B financing.

**Ventrus Biosciences Inc.** raised \$45 million in a public stock offering.

### Deals

**Allergan Inc.** acquired dermatology company **Viccept Therapeutics Inc.** for \$275 million.

**AMAG Pharmaceuticals Inc.** and **Allos Therapeutics Inc.** are merging in a \$686 million all-stock deal.

**BioSante Pharmaceuticals Inc.** licensed a melanoma vaccine to the John P. Hussman Foundation.

**Icagen Inc.** is being acquired by partner **Pfizer Inc.** for \$56 million.

**NeoStem Inc.** acquired privately held stem cell firm **Amorocyte Inc.** for \$18 million.

**Vical Inc.** signed a potential \$130 million deal with **Astellas Pharma Inc.** for TransVax in transplant.

### ... And More

**AstraZeneca plc's** Brilinta (ticagrelor) gained FDA approval for acute coronary syndromes.

**AstraZeneca plc** and **Bristol-Myers Squibb Co.**'s diabetes drug dapagliflozin got rejected by an FDA advisory panel.

**Dynavax Technologies Corp.**'s hepatitis B vaccine Heplisav met its Phase III endpoints, but had a manufacturing inconsistency.

**Exelixis Inc.** said partner **Bristol-Myers Squibb Co.** handed back rights to XL281.

**Nabi Biopharmaceuticals Inc.**'s smoking cessation vaccine NicVAX failed Phase III.

**Transcept Pharmaceuticals Inc.** is eliminating 45 percent of its work force.

## Form 10

*Continued from page 1*

company would either need to raise money privately ahead of listing its shares, or it would need to do a public offering or a PIPE once it was listed. The public listing would certainly provide more financing options, but initial illiquidity could make the investment less appealing.

Yet there are benefits to the Form-10 pathway. With even Phase III biotechs getting a chilly reception from IPO investors, the Form 10 offers an option to earlier-stage firms like Coronado, which is still in preclinical stage with its autoimmune and cancer programs, although it aims to have both in Phase II trials by early next year.

In a recent report, Grimaldi noted that the Form-10 pathway virtually eliminates exposure to market risk and greatly lowers transaction costs compared with an IPO. It also avoids the baggage that often comes with a reverse merger: unhappy shareholders, hidden liabilities and low market capitalization.

Coronado found those benefits appealing as well. The biotech didn't need money because it had just raised \$25.8 million in a Series C financing, and it didn't need help building a shareholder base because it had more than 500 investors already.

"Coronado is in a position not a lot of companies are in," Stoller said. ■

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*Later rather than Sooner*

## Targeted Therapy Resistance: No Reason to Stop Treatment?

By Anette Breindl  
Science Editor

From old stalwarts like Gleevec (imatinib, Novartis AG) to new stars like vemurafenib (PLX4032/RG7204, Plexxikon Inc./Roche AG), targeted therapies work well until they don't. Sooner or later, resistance – in the form of secondary mutations – rears its ugly head.

But an ounce of prevention may do a lot of good in delaying the appearance of such mutations. And surprisingly, even after mutations have emerged, such drugs continue to be useful in delaying tumor progression.

Those are the conclusions of a recent study, published in the July 6, 2011, issue of *Science Translational Medicine*.

In their work, the authors looked at EGFR-mutated lung tumors, which are the targets of Iressa (gefitinib, AstraZeneca plc) and Tarceva (erlotinib, Astellas Pharma Inc. and Roche AG).

The majority of EGFR-mutated tumors at first respond well to EGFR inhibitors. But sooner or later mutations develop. About half of the time, those mutations are at one specific site and lead to the replacement of a threonine with a methionine at position 790 of the EGF receptor – the T790M mutation.

It is the drug itself that puts selective pressure on the tumor, favoring escape mutations. But such selective pressure can be minimized through alternative dosing strategies. Indeed, while the drugs themselves are rationally designed, “you can come up with much more rational treatment strategies,” co-author Vincent Miller, a thoracic oncologist at Memorial Sloan-Kettering Cancer Center, told *BioWorld Insight*.

In their paper, the authors treated cell lines that were genetically identical except for the presence or absence of the T790M mutation, and used them to test different dosing strategies that might prevent the emergence of resistance. The most promising such strategy appears to be combining low daily doses of erlotinib with intermittent higher-dose pulses.

Surprisingly, their results also suggested that continuing treatment with erlotinib after resistance has developed could be indicated clinically.

The reason is that a tumor that contains cells with the T790M mutation does not contain only cells with the T790M mutation: “One of the key pieces is that the tumor is a mixture of cells that have just the original mutation, and those that have the second mutation, the T790M site, as well,” Miller said.

And if erlotinib treatment is stopped for such a tumor, the cells with just the original EGFR mutation will undergo a growth spurt of sorts. Such cells already divide more often than those with the T790M mutation, which makes cells resistant to EGFR inhibitors at the price of slowing their growth.

Given the oft-bemoaned costs of targeted therapies, the idea of continuing to give a patient a drug to which resistance has developed might seem like it will crash and burn for economic reasons no matter what its scientific merits.

But both Miller and Bruce Johnson, head of the thoracic oncology program at Dana Farber Cancer Institute, said that the costs of erlotinib could actually turn out to be less than those of alternative treatments.

At about \$3,000 per month, erlotinib is expensive, but not in the same stratospheric region as some monoclonal antibodies. “Standard chemo,” Johnson told *BioWorld Insight*, “costs a lot more than that.”

Partly because it is an intravenous drug as opposed to a pill, Alimta (pemetrexed, Eli Lilly and Co.), the primary chemotherapy drug for lung cancer, is itself no bargain-basement drug: It costs about \$5,000 per dose, and is given every three weeks.

Add to that the fact that severe toxicities are, Johnson said, “a third less frequent” with erlotinib than with chemotherapy, and the comparison looks better still.

Testing the paper's suggestions clinically will take at least two years. But Miller agreed that whatever the hurdles to its practical use are, the cost of treatment is not likely to be its death knell. Continuing targeted treatment, he agreed with Johnson, “might be more effective from a financial standpoint.” ■

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