

The A-List: 2009's Trend-Shaping Series A Financings

New company creation slipped significantly in 2009 as venture capitalists conserved capital and supported existing portfolio companies. In biopharmaceuticals, corporate venture got in at the ground floor while device start-ups continued to see stronger support from smaller, regional investors than from traditional VCs.

BY CHRISTOPHER MORRISON AND TOM SALEMI

The question many venture investors were asking themselves throughout 2009 seems to be, "is it safe to come out yet?" And that cautious approach to investing embraced by many VCs has translated into a significant dip in Series As. Still, START-UP has identified a baker's dozen to keep an eye on in 2010 and beyond. (See Exhibit 1.)

There were 60 new Series A investments in biopharma firms in 2009, down sharply from 2008 and 2007, which each boasted more than 80 deals. The total value of all biopharma Series As fell by about one third, to about \$870 million, although the average round size continued to hover around \$15 million. (See Exhibit 2.) Meanwhile, illustrating VCs' priorities during uncertain times, at least a dozen biopharma companies that had raised A rounds prior to 2009 added to those rounds. If in 2008 flat rounds were the new up, in 2009 second tranches were the new flat rounds. (See "Reacting to the Crisis: Biotech Venture Capital's Plan B," START-UP, December 2008.)

Those companies that did manage to raise their first significant private capital followed several familiar paths. There were pharmaceutical spin-offs, and big bets on proven management teams. Anti-infectives and oncology plays again dominated the newco landscape; alongside biologics platforms these therapeutic spaces show no signs of going out of style. At the other end of the spectrum, cardiovascular and metabolic disease start-ups were absent from the 60 new A rounds of 2009, reflecting a difficult regulatory and reimbursement climate for drugs in these areas.

For the first time in several years there were no RNA-based drug developers receiving VC-backed Series As (though **Miragen Therapeutics Inc.**, one of 2008's A-Listers, did close a second tranche to its maiden round). (See sidebar, *Where Are They Now? Catching Up With the Classes of 2004-2008, Biopharmaceuticals.*) Only **Regulus Therapeutics Inc.**—a microRNA-focused joint

venture between **Alnylam Pharmaceuticals Inc.** and **Isis Pharmaceuticals Inc.**—pulled in a Series A, and (for now) Alnylam and Isis, which each contributed \$10 million, are keeping their investment to themselves.

And strategic investors with more formal corporate venture capital ambitions were out in force in 2009, a phenomenon that was all the more pronounced thanks to traditional VCs' reluctance. (See "Corporate Venture Takes Center Stage," START-UP, May 2009.) Old standbys such as **GlaxoSmithKline PLC's** SR One have been among the most active dealmakers this year, but newer entrants such as the Novartis Option Fund have also made an impact at the earliest stages in the biotech life cycle.

The medical device industry, meanwhile, saw a serious drop both in dollars committed to Series A rounds and in the number of deals done. Only 35 medical device start-ups raised Series A rounds last year, a 20% drop from the 44 raising capital in 2008. More troubling, however, is the 40% drop in dollars, from \$289 million to a paltry \$167 million, the lowest figure we've recorded since 2005.

To be sure, venture-backed companies overall took in fewer dollars and closed fewer deals, drop-offs of 41% and 49%, respectively, according to Dow Jones VentureSource. But that database suggests the device industry was one of the stronger sectors. The total dollars committed to all device companies fell only 24%, while the number of deals done slipped by only 9%.

This incongruity suggests that venture capitalists are steering their dollars away from early-stage companies, either committing them to their existing companies or looking for more established later-stage opportunities. (In fact, eight medical device companies padded more capital into Series A rounds they'd raised previously rather than attempting to raise a Series B.)

Medical device companies once again received stronger support from regionally focused investment capital funds and angels groups—the two asset classes that have had to fill any venture gap as established coastal VCs reserve their capital. We also saw strong participation from European firms, such as Broadview Ventures' commitment to **CardiAQ Valve Technologies Inc.**, a mitral valve company, and the strong European syndicate backing of **CeQur SA**, which is developing a disposable insulin pump. Both companies boast

European roots. It's worth noting that a third selected company also comes from abroad. **Pfizer Inc.** teamed with Johnson & Johnson Development Corp. to supply a Series A round to **NovoCure Ltd.**, an Israeli-based company that established US operations to test an electrical field generator that could kill cancer.

Paylon Medical Corp., meanwhile, represents the enormous interest venture capitalists paid to combating pain. The company, which is testing a system to deliver drugs directly into the spine, was one of six pain-oriented companies raising Series A rounds in 2009. Paylon's

Exhibit 1

The 2009 A-List

COMPANY	AMOUNT RAISED (MILLIONS)	DEAL DATE (2009)
Alios BioPharma	\$32	February
CardiAQ Valve Technologies	\$6.5	December
CeQur SA	\$29.6	December
Clovis Oncology	\$145	May
Durata Therapeutics	Undisclosed	December
Flexion Therapeutics	\$42	December
Genocea Biosciences	\$23	February
Heptares Therapeutics	£21	February
Integrated Diagnostics	\$30	October
Kolltan Pharmaceuticals	\$40	January
NovoCure	Undisclosed	September
On-Q-ity	\$26	November
Paylon Medical	\$24	April

SOURCE: Elsevier's *Strategic Transactions*

Exhibit 2

By the Numbers

(\$mm)

	2004	2005	2006	2007	2008	2009
Biopharma						
Total Series A	866.1	1003.7	1018.7	1159.9	1,207.5	879.8
Average Series A	12.6	23.3	19.6	15.1	15.5	14.9
Diagnostics						
Total Series A	30.9	4.3	117.4	153.6	82.2	140.1
Average Series A	7.7	4.3	16.8	8.5	5.9	11.7
Medical Devices						
Total Series A	98.3	100	244.2	197	289	167.5
Average Series A	9.8	8.3	9.3	8.2	7.1	4.79
All Companies						
Total Series A	995.3	1108	1380.3	1508.5	1578.7	1186.6
Average Series A	12	19.8	16.2	12.4	11.9	11.2

SOURCE: Elsevier's *Strategic Transactions*

round was the largest, totaling \$24 million. Companies with neurostimulation technology and those targeting obesity continued to be popular areas of support, while only one ophthalmology company, **ForSight Vision4 Inc.**, a spin-out of the Forsight Labs LLC incubator, raised capital.

ALIOS BIOPHARMA

The antiviral specialist **Alios BioPharma Inc.** pulled in a structured Series A that comprised an \$8 million down payment from Novo Ventures, Novartis Ventures and Roche Venture Fund in February 2009. That figure was due to increase to \$24 million, but in June GSK's SR One joined the syndicate, boosting the haul to \$32 million.

Alios' round reflects heightened pharmaceutical interest in virology and could be considered the poster-financing for the rise of corporate venture capital funds. CVCs have filled at least some of the gap left by the shrinking pool of capital available from more traditional VCs hit hard by the global financial crisis. For example, according to Russell Greig, who heads up SR One, the investor plans to do six to eight equity deals annually: that's certainly more than some of the once-higher-flying traditional VCs can manage. Novo isn't quite a CVC, though it is somewhat related to Novo Nordisk through the Novo Foundation, but it's close enough for *START-UP* to marvel that four out of four investors have corporate ties. According to Elsevier's *Strategic Transactions*, 20% of all biopharma Series As in 2009 included one or more corporate investor, and 40% of the top 20 deals by cash amount.

Alios' attempts to engineer an improved interferon drug are complemented by an effort to develop an oral version of the broad-spectrum antiviral as well. CEO and co-founder Lawrence Blatt, PhD, has built a career in the interferon and hepatitis C areas, moving from **Amgen Inc.**, where he ultimately led development of the "consensus interferon" *Infergen*, on to **InterMune Inc.**, where he was CSO and led the team that invented that biotech's HCV protease inhibitor ITMN-191 (now partnered with **Roche**). (See "Alios BioPharma Inc.," *START-UP*, June 2009.)

The biotech has plenty of competition on the interferon front. **ZymoGenetics Inc.** licensed global rights to its interferon lambda program to **Bristol-Myers Squibb Co.** in January 2009 for \$85 million up front—not bad for a Phase I asset. **Biolex Therapeutics Inc.** (interferon alfa; *Locteron*) and **Human Genome Sciences Inc./Novartis AG** (albinterferonalfa-2b; *Zalbin*) are in mid-stage development and registration, respectively. (Biolex took in \$60 million, principally for *Locteron* development, from a group led by Clarus Ventures and Orbimed Advisors in October 2008.)

Alios BioPharma Inc.

Embracing Corporate Venture in Virology

\$32 million, February/June 2009

Novo Ventures, Novartis Venture Fund, Roche Venture Fund
SR One

CARDIAQ VALVE TECHNOLOGIES

When CardiAQ Valve Technologies Inc. announced raising its \$884,000 seed funding in May of last year, CEO J. Brent Ratz suggested the company would do for mitral valve repair what CoreValve Inc. did for aortic stenosis. That's quite a comparison for a start-up company to make given the \$700 million acquisition of CoreValve by **Medtronic Inc.** a year ago, but he wasn't the only one who noticed the resemblance.

Investor Rob Michiels and the same group of angel investors who initially backed CoreValve joined seed round investors Broadview Ventures to supply the company with a \$6.5 million Series A. The mitral valve repair market is poised for growth. For years it's taken a back seat to finding percutaneous treatments for the aortic market, largely because repairing the mitral valve is a more difficult procedure. Up until recently, aortic valve replacement has drawn the most interest from larger players like Edwards Lifesciences Corp. and CoreValve, which became Medtronic CoreValve LLC after the acquisition.

CardiAQ's percutaneous valve replacement system may someday significantly reduce the risks of these procedures with a catheter-based system of delivering a new valve. The company is developing a unique fixation mechanism and a novel delivery catheter that will allow surgeons to accurately and securely implant a new mitral valve within a beating heart, thus avoiding open-heart surgery. If the company is successful in developing its replacement valves, it could someday draw comparison to another well-known valve company, **Evalve Inc.**, which **Abbott Laboratories Inc.** acquired last year for \$410 million.

CardiAQ Valve Technologies Inc.

Pursuing Percutaneous Mitral Valve Repair

\$6.5 million, December 2009

Broadview Ventures, Rob Michiels, angels

CEQUR SA

People with type 2 diabetes (T2D), the more common form of the disease, don't bear the same risk of hypoglycemia, ketoacidosis, and death as the smaller group of patients with the type 1 form of the disease. However, T2D may lead to blindness, amputation, and other serious complications if the condition goes untreated. And there's the rub. Because the risk for injury and disease isn't as immediate, type 2 diabetics don't share the vigilance in measuring glucose levels of their type 1 counterparts. People who might require up to four injections of insulin a day to stay healthy simply don't comply, putting themselves in enormous jeopardy when they get older.

This lackadaisical attitude is creating an enormous opportunity for medical device companies such as CeQur SA. (See "Will Simpler Devices Tap the Largest Diabetes Market?" START-UP, November 2008.) More than a dozen companies are working to develop easier methods of delivering insulin in a bid to tap into the 48 million type 2 diabetics, or, more specifically, the eight million who currently use insulin to control T2D.

CeQur secured an additional 10.3 million Swiss francs (\$10 million) to round out a Series A round at 31.7 million Swiss francs (\$29.6 million). Proceeds from the financing will enable the company to obtain CE mark approval for CeQur's insulin infuser, introduce the product to market in Europe, and file the IDE necessary for a US 510(k) approval.

The insulin infuser is a small device that someone might wear on his or her stomach or some other discreet location. Through a soft canula, the device delivers a steady supply of basal insulin, the background insulin that the body consistently needs. At mealtime, a button on the device can deliver bolus insulin, the extra dose necessary to properly process food. (See "CeQur: Conforming to the Lifestyle of the Type 2," START-UP, November 2008.)

CeQur's infuser device was created by Danfoss AS, a large, global Danish industrial products group that developed fluid transfer technology. Upon retiring as CEO of **Haemonetics Corp.** and subsequently advising Warburg Pincus on diabetes deals, Jim Peterson joined CeQur as CEO. In October, CeQur added Eric Milledge as chairman. Milledge, a 34-year veteran of J&J, most recently served as company group chairman of **Lifescan Inc.**, the market leader in blood glucose monitoring. Milledge led the acquisitions of **Animas Corp.** and Inverness Medical Technology, helping to build J&J's diabetes business.

CeQur SA**Making Insulin Delivery Easy****\$29.6 million, December 2009****BMC Ventures A/S, Endeavour Vision SA, Schroder & Co Bank AG, and Venture Incubator AG***Making Insulin Delivery Easy***CLOVIS ONCOLOGY**

It's the largest Series A funding ever for a biotech, and the size of **Clovis Oncology Inc.**'s deal may have had observers rubbing their eyes. But the \$145 million Series A has a familiar look. The funding, from Domain Associates, New Enterprise Associates (NEA), Versant Ventures, Aberdare Ventures, Abingworth, Frazier Healthcare Ventures, ProQuest Investments, and the company's management team, reunites the team behind Pharmion (which was bought by **Celgene Corp.** for \$2.7 billion in 2008).

All of those firms (with the one exception of Frazier) had ties to Pharmion. Pharmion founder and CEO Patrick Mahaffy is at the helm of Clovis. The biotech aims to in-license early-stage oncology assets and take them through to the market. It inked its first deal this past November, when it paid **Clavis Pharma ASA**, a Norwegian biotech, \$15 million up front and potentially \$365 million on the back-end for rights in Europe and the Americas to a reformulated version of **Eli Lilly & Co.**'s gemcitabine (*Gemzar*), called CP-4126. The Phase II drug could benefit pancreatic cancer patients who don't respond to Lilly's version because they are under-expressing the transfer protein that shepherds *Gemzar* into cells. (See "Clovis Taps Into Rich 'A' Round, Grabs Licensing Rights to Improved Gemcitabine," The Pink Sheet DAILY, November 24, 2009.)

Surely Clovis investors' largesse will bring in further projects, and few would bet against Mahaffy and the company's pedigree. It plans to IPO within the same time frame as Pharmion—about three years from foundation. But big name backers and lots of cash aren't a slam dunk recipe for start-up success. One former A-Lister, **Verus Pharmaceuticals Inc.**, began life similarly sanguine (and with \$98 million) in 2005 but has since been dismantled.

Clovis Oncology Inc.**Let's See You Do That Again!****\$145 million, May 2009****Domain Associates, New Enterprise Associates, Versant Ventures, Aberdare Ventures, Abingworth, Frazier Healthcare Ventures, ProQuest Investments, Clovis management**

DURATA THERAPEUTICS

Another year, another Pfizer spin-off on *The A-List*. But this year's entrant has a very different feel from the genesis of the Japanese biopharma **RaQualia Pharma Inc.**, Pfizer's first effort. (See "*The A List: 2008's Trend Shaping Series A Financings*," START-UP, January 2009.)

Durata Therapeutics Inc. was formed in December 2009 when New Leaf Venture Partners, Domain Associates, Aisling Capital, Sofinnova Ventures and Canaan Partners paid Pfizer an undisclosed amount to buy out the assets of the former Vicuron Pharmaceuticals. Pfizer, which does not hold a stake in the new biotech, originally bought anti-infectives-focused Vicuron in 2005 for \$1.8 billion, only to see the long-acting antibiotic dalbavancin languish in late-stage development and the anti-fungal anidulafungin (*Eraxis*) perform woefully in the marketplace. (See "*Pfizer-Vicuron: Fill Pipeline, Minimize R&D Expense*," IN VIVO, July 2005.)

Pfizer will hang on to *Eraxis* but dalbavancin is now Durata's singular challenge. The drug candidate remains in Phase III, where it has been tested as a once-weekly treatment for acute bacterial skin and soft tissue infections. Durata knows the history: former Vicuron CFO and EVP Dov Goldstein, MD, is now partner at Aisling and former Vicuron CEO George Horner is now executive partner at Sofinnova. Both men are members of the Durata board.

Vicuron's aren't the only assets Pfizer jettisoned in late 2009. Also in December the Big Pharma licensed worldwide rights to the stalled HDL raiser ApoA-1 Milano to **The Medicines Co.** for \$10 million up front. Pfizer originally gained access to that asset when it spent \$1.25 billion to buy **Esperion Therapeutics Inc.** in 2003. Other pharma have parted with assets as well; Roche spun out pain-focused **Afferent Pharmaceuticals Inc.** in December with backing from Third Rock, Domain, Pappas and New Leaf, for example. (See also "*Flexion Therapeutics*," below.)

Durata Therapeutics

Pfizer Gives Up on Vicuron

Undisclosed investment, December 2009

New Leaf Venture Partners, Domain Associates, Aisling Capital, Sofinnova Ventures, Canaan Partners

FLEXION THERAPEUTICS

Formed by the former Eli Lilly executives who ran the company's experimental development group Chorus, **Flexion Therapeutics Inc.** aims to do for itself what it was able to do for Lilly: faster, more predictable drug development. (See "*Lilly's Chorus Experiment*," IN VIVO, May 2007.) And because it is going after pharma's deprioritized assets, it should get its starting material on the cheap.

In October Flexion announced it had raised \$33 million in a Series A led by Versant Ventures with participation from 5AM Ventures and Sofinnova Partners; in December an undisclosed fourth investor boosted the round to \$42 million. And in January 2010, the company will announce it has in-licensed a handful of compounds from multiple pharma sources: **AstraZeneca PLC**, **Merck KGAA's Merck Serono SA**, and an undisclosed Big Pharma. (See "*Flexion Exploits Big Pharma as Discovery Supplier*," IN VIVO, January 2010.) Those deals are structured in a variety of ways—from outright ownership to pharma claw-backs.

Flexion's model is timely. Pharmaceutical companies find themselves cutting back on development in particular therapeutic spaces even as their discovery engines are collectively humming. Cost-savings initiatives and industry consolidation leave more compounds than ever ripe for the taking by Flexion and others (like Durata, above, or Swiss biotech **Debiopharm Group**, which just this month signed a deal with Pfizer to test Pfizer's tremelimumab antibody in a biomarker-defined subset of melanoma patients; the candidate had failed a previous Phase III trial).

Now that Flexion has demonstrated it can bring molecules in-house (which was not an easy process, the company apparently rejected more offerings than it anticipated), the challenge is to shepherd those candidates through to proof-of-concept and secure out-licensing deals. Lilly's experience with Chorus should bolster Flexion's prospects—the group has succeeded in the eyes of Lilly management and is being replicated in Indianapolis. Further, Lilly has inked a joint venture with India-based **Jubilant Organosys Ltd.** to combine Chorus' rapid-POC model with Jubilant's lower cost structure.

Flexion Therapeutics Inc.

Faster, Cheaper, More Predictable

\$42 million, December 2009

Versant Ventures, 5AM Ventures, Sofinnova Partners

GENOCEA BIOSCIENCES

In a year dominated by concerns about swine flu it should come as no surprise that infectious diseases and vaccines in particular remained a popular investment choice for early-round cash. **Genocea Biosciences**, which discovers and develops vaccines against the pathogens living inside phagocytes or other cells (intracellular pathogens), such as chlamydia and tuberculosis, is our pick of the bunch, with a \$23 million February 2009 Series A led by SR One with participation from Auriga Partners, Cycad Group, Alexandria Real Estate Equities, Lux Capital Management, Polaris Venture Partners, and Morningside Ventures.

Genocea's T-cell directed antigen discovery platform starts by cross-referencing people who are protected from disease against those who are not and essentially replicates the intracellular immune system in the lab, according to CEO Mustapha Bakali. The company's proprietary antigen library and screening technology allows it to identify why a protected cohort is protected, and what antigens it is responding to that others are not, he told *START-UP*. The biotech has preclinical candidates against chlamydia and streptococcus as well as several undisclosed preclinical candidates. The chlamydia project is based on the work of scientific founder Darren Higgins, PhD, whose lab at **Harvard Medical School** discovered 14 antigens that have been exclusively licensed to Genocea. The pneumococcus project is partially funded by PATH, a global non-profit, and is being developed in conjunction with Children's Hospital Boston.

Also pulling down Series As were vaccines plays **Inviragen Inc.** (\$4.4 million of a potential \$15.3 million Series A financing to 24 investors including Charter Life Sciences, Venture Investors, Bio*One Capital, and Phillip Private Equity) and flu-focused **Vivaldi Biosciences Inc.** (\$18.85 million co-led by Bay City Capital and NGN Capital, joined by the New York City Investment Fund and Alexandria Real Estate Equities).

HEPTARES

GPCRs may make good drug targets—roughly 150 are well validated as such—but these transmembrane receptors don't exactly behave well in the laboratory setting. Removing them from the cell membrane to be poked and prodded and sized up for chemical intervention has been a challenge: the receptor essentially falls apart, or is at least misshapen, and therefore can't be examined structurally as other proteins can, via x-ray crystallography.

Enter **Heptares Therapeutics Ltd.** and its *Stabilized Receptor (StaR)* technology. The UK biotech raised £21 million (\$30 million) in February 2009 in a Series A led by Clarus Ventures with participation from Novartis Option Fund (NOF) and MVM Life Sciences Partners to develop and exploit a technique that allows it to remove stable GPCRs from the cell membrane. The technology has drawn the attention of **Novartis AG**—which along with its investment has signed up Heptares to produce small molecules against an undisclosed GPCR target. The biotech could get up to \$200 million in up-front and milestone payments.

The alliance with Heptares is Novartis' second GPCR partnership via its option fund (after a similar deal with **Ascent Therapeutics Inc.** in December 2008; the NOF also invested in Ascent's 2007 A round as well as **Forma Therapeutics Inc.**'s January 2009 \$25 million A round). Elsewhere in GPCR drug discovery company formation, ARCH Venture Partners, Flagship Ventures, Lilly Ventures, and Venrock poured \$25 million into the February 2009 Series A of **Receptos Inc.**, which subsumed the assets of 2008 A-List firm Apoptos.

INTEGRATED DIAGNOSTICS

Integrated Diagnostics Inc., a start-up with direct ties to the **Institute for Systems Biology** (ISB) entrepreneur Leroy Hood, MD, PhD, aims to develop a new generation of exquisitely precise diagnostic tests based on biomarkers present in the bloodstream. Founded in 2008, Integrated Diagnostics operated in stealth mode until October 2009, when it announced a \$30 million Series

Genocea Biosciences

T-cell Directed Antigen Discovery

\$23 million, February 2009

SR One, Auriga Partners, Cycad Group, Alexandria Real Estate Equities, Lux Capital Management, Polaris Venture Partners, Morningside Ventures

T-cell Directed Antigen Discovery

Heptares Therapeutics Ltd.

Stabilizing GPCRs for Drug Discovery

£21 million, February 2009

Clarus Ventures, Novartis Option Fund, MVM Life Science Partners

A with backing from lead investor InterWest Partners, as well as the Wellcome Trust, and dievini Hopp Biotech holding GMBH.

As one might expect given the start-up's link to Hood, the company is taking a systems biology approach to the development of its proprietary biomarker assays. Based on the theory that diseases such as diabetes and cancer result from global changes in the body's network of proteins and genes, Integrated Diagnostics aims to create tests incorporating tens to hundreds of specific biomarkers from 50 major organs present at the earliest stages of the disorders. The start-up appears to be setting its sights first on the development of a lung cancer test thanks to intellectual property that arose from a public-private partnership between ISB and the country of Luxembourg to develop biomarkers to detect that disease.

Integrated Diagnostics Inc.

All Systems Go

\$30 million, October 2009

InterWest Partners, Wellcome Trust, dievini Hopp Biotech

KOLLTAN PHARMACEUTICALS

Oncology continues to dominate biopharmaceutical Series A investments, with more than a dozen cancer-focused companies securing first-round investments in 2009. **Kolltan Pharmaceuticals Inc.**'s haul was second only to Clovis' (*see above*). But unlike its competitor, Kolltan is pursuing drug discovery from scratch.

The company raised \$35 million in a January 2009 A round that included backing from Purdue Pharma, HBM Capital Partners, the Pritzker/Vlock family, and other private investors; it tacked on \$5 million in a second close in August.

Kolltan Pharmaceuticals Inc.

Disarming the Resistance

\$40 million, January 2009

Purdue Pharma, HBM Capital Partners, the Pritzker/Vlock family and other private investors

Kolltan spun out of Yale University and is based on the research of co-founder and Yale pharmacology professor Joseph Schlessinger, PhD. Schlessinger's lab has elucidated a mechanism by which receptor tyrosine kinases can become resistant to existing cancer drugs, and Kolltan, armed with that IP, aims to design small molecules and monoclonal antibodies such that they are unaffected by that resistance.

NOVOCURE

Corporate investors Pfizer and Johnson & Johnson Development Corp. certainly aren't the strangest of bedfellows, but their co-investment in NovoCure is rather peculiar. NovoCure is a medical device company, an unusual investment target for a pharmaceutical giant like Pfizer.

That said, NovoCure isn't your typical device company. Like many device start-ups, NovoCure is developing an energy-based therapeutic. But the company isn't employing energy to ablate tissue, stimulate nerves or reset an irregular heartbeat. NovoCure is out to kill cancer cells.

The firm is hoping to harness a very specific frequency of electrical energy. Many devices today use electrical energy. Low-frequency devices such as defibrillators and other stimulators cause muscles to contract; higher-frequency energy can literally cook tissue, making it useful in ablation. NovoCure is working somewhere in between, where electric stimulation was thought to have no impact on living tissue. The company's technology is based on the work of Yoram Palti, MD, PhD, a former professor of the **Technion Israel Institute of Technology**.

NovoCure Ltd.

Killing Cancer with Electricity

Round size undisclosed, September 2009

Index Ventures, Johnson & Johnson Development Corp., Pfizer Inc., WFD Ventures

NovoCure's *Novo-TTF-100A* device administers a very low intensity, alternating electric field through an electrode on the skin. The fields—which the company is calling Tumor Treating Fields or TTFs—wash over all the tissue but affect only cells at the moment of division. The company says

the TTFs cause the building blocks of the new and old cells to pile up in such a way that the cells and their building blocks physically break apart. *Novo-TTF* treatment has been found to slow—and even reverse—progression of cancer.

NovoCure has successfully run the technology through several smaller clinical trials on different types of cancer. Now it's enrolled 236 patients in a multi-center, randomized, pivotal clinical trial studying the effect of the electric fields on recurrent diagnosed brain-tumor-causing glioblastoma multiforme (GBM) compared with standard-of-care chemotherapy. The results of this trial will be presented to the FDA as part of a PMA application planned for early next year. Meanwhile, NovoCure intends to enroll up to 283 patients in a second trial with two-thirds of the patients undergoing *Novo-TTF* and chemotherapy and one-third receiving just standard chemotherapy.

ON-Q-ITY

One of the leading diagnostic players to emerge in 2009 was Waltham, MA-based **On-Q-ity Inc.**, formed from the wreckage of two private start-ups, Collective Dx and the DNA Repair Co. Both predecessors were Mohr Davidow portfolio companies that struggled to raise Series B money in 2009's tepid financial climate. Mohr Davidow, which has made a concerted effort to invest in molecular diagnostic players, participated in the first-round financing for the new start-up, which ultimately pulled in \$26 million. Other investors include Bessemer Venture Partners, Physic Ventures, Northgate Capital (also a Collective Dx investor), and Atlas Venture. On-Q-ity seems more likely to succeed than its two predecessors, attracting some star management power, including president Mara Aspinall, formerly at **Genzyme Corp.**'s **Genzyme Genetics**, as the start-up's president and CEO. The company is developing tests to diagnose and monitor oncology therapies, building on technologies originally developed at **Massachusetts General Hospital**, the **Dana-Farber Cancer Institute** and the **Massachusetts Institute of Technology** that detect and monitor rare circulating tumor cells from the blood of cancer patients. In addition to DNA repair biomarkers that predict a patient's likelihood to develop resistance to a particular medicine, On-Q-ity's intellectual property includes microfluidic chips capable of capturing elusive CTCs. (See our profile of *On-Q-ity* in this issue.)

On-Q-ity Inc.

Monitoring CTCs

\$26 million, November 2009

Mohr Davidow, Bessemer Venture Partners, Physic Ventures, Northgate Capital, Atlas Venture

PAYLON MEDICAL

Medical device investors and entrepreneurs continue to target markets served almost exclusively by pharmaceuticals, including pain management. Paylon Medical Corp. is one of four medical device companies raising Series A rounds to further product development programs to combat pain.

Established in 2007, Paylon Medical is built around technology licensed from **Fresenius SE**. The company is developing a programmable implant that delivers pain drugs directly to the spine for the treatment of chronic pain, spasticity and other potential CNS conditions. As is the practice of most device companies targeting conditions treated with drugs, Paylon is developing its drug delivery device for patients in chronic pain who haven't responded to existing treatments such as oral medication or physical therapy. This can be up to 20% of the 76 million Americans who suffer with chronic pain, defined by the company as lasting six months or longer. According to Paylon, chronic pain affects more Americans than heart disease, diabetes, and cancer combined. Medtronic's *SynchroMed* implantable infusion system currently dominates this market.

Led by CEO David Present, MD, Paylon will use the Series A money to run a multi-site clinical trial of its device. Glen Kashuba, president of **Biomet Inc.**'s Biomet Trauma and Biomet Spine divisions, was appointed to the company's board. Other pain management companies raising Series A rounds include neurostimulation companies **Current Solutions LLC** (electrotherapy devices for pain management), **Neuros Medical Inc.** (a device for chronic pain that uses high-frequency alternating currents to stop sensory and motor nerve activity in the peripheral nerve system), and **MicroTransponder Inc.** (a wireless neuromodulation device).

Paylon Medical Corp.

Getting to the Root of Pain

\$24 million, April 2009

Baird Venture Partners, Hambrecht & Quist Capital Management, Fountain Healthcare Partners, BB Biotech Ventures, Cross Atlantic Partners, and Arcus Ventures, Nextech Ventures

Killing Cancer with Electricity

Getting to the Root of Pain

Where Are They Now? Catching Up With the Classes of 2004–2008

I. Biopharmaceuticals

Even though it wasn't quite a quiet year for biopharma companies from A-Lists past, things didn't really heat up for our alumni until late in 2009. December saw the year's only two exits for the group, with **AstraZeneca PLC** and **Forest Laboratories Inc.** teaming up to acquire **Novexel SA** (Class of 2004) for \$350 million up front plus earn-outs and **Movetis NV** (2007) successfully tapping the public markets for nearly €98 million (\$147 million) in the year's biggest biotech IPO. The latter deal earned the Exit/Financing Deal of the Year from readers of *The IN VIVO Blog*. (See "The Merger/License Dance of AstraZeneca, Forest and Novexel," and "Best of The IN VIVO Blog," both in this issue.)

Meanwhile, a few other companies were bought or ceased operations in deals that didn't represent good exits for their backers. **Receptor BioLogix Inc.** (2006) assets were acquired by **Symphogen AS** in January. **Verus Pharmaceuticals Inc.** (2005) had previously sold off its assets and investors were essentially waiting on milestones from partner AstraZeneca. Those milestones seem unlikely to materialize since AZ has in-licensed a competing compound, which is the subject of a lawsuit between the two companies. (See "From Verus to Meritage: A Biotech Prototype for Tough Economic Times," *START-UP*, March 2009 and "Verus Sues AZ for \$1.28B Over Deals to Develop Pediatric Asthma Drug," *The Pink Sheet DAILY*, May 27, 2009.) Dermatology play **Magen Biosciences Inc.** was bought by contract researcher **Pharmaceutical Product Development Inc.** in April for \$14.5 million.

Perhaps most interestingly on the non-exit front, 2008 A-Lister Apoptos morphed into a new start-up only months after its original Series A. In fact, Apoptos nearly achieved a remarkable and unprecedented feat—it almost became the first company to make *The A-List* two years in a row. Let us explain. In November 2009, **Receptos Inc.** secured \$25 million in Series A funding from Arch Venture Partners, Flagship Ventures, Lilly Ventures, and Venrock. Venrock and Arch were among Apoptos' backers in its structured \$28 million May 2008 Series A, \$5 million of which was rolled into Receptos' A round when that company bought Apoptos in June 2009. In case you haven't guessed, Receptos is essentially Apoptos 2.0, with Apoptos management at the helm, including chairman/CEO William Rastetter, PhD. (See "Newly Funded Receptos Bets on the Safety of Its Oral MS Drug," *The Pink Sheet DAILY*, November 23, 2009.)

Other A-Listers tapped their venture backers for new cash. **Lux Biosciences Inc.** (2005) followed Phase III data on lead uveitis compound oral voclosporin (*Luveniq*) with a \$50 million insider round to pursue registration and launch. Another ophthalmology play **Alimera Sciences Inc.** (2004) added \$15 million in two extensions to its Series C from March 2008 and prepared to file an NDA for its *Iluvien* insert to deliver fluocinolone acetonide diabetic macular edema compound in 2010. **Nabriva Therapeutics Forschungs GMBH** (2005), the Sandoz spin-out, raised a €15 million B round in October, and signed on a new CEO, former CAT founder David Chiswell. Other fundraisers

included **Helicos Biosciences Inc.**, **HistoRx Inc.** (both 2004), and **Helixis Inc.** (2007). **Sequel Pharmaceuticals Inc.** (2007) raised \$3 million in debt in August, **Cerulean Pharma Inc.** (2007, nee Tempo) pulled in a \$10 million Series B in July after licensing a Phase II anticancer candidate from **Calando Pharmaceuticals Inc.** (along with rights to a delivery platform) for \$2.4 million up front in June. **23andMe Inc.** (2007) likewise landed a partner and some new cash. It signed a rare diseases partnership with **mondoBiotech AG** in January and raised a \$12.6 million Series B in June. And **f-star Biotechnology Research & Development Co.** (2007), one of a dozen companies to top-up Series As in 2009, extended its Series A by €8 million in early January.

Anaphore Inc. (2008) tackled two trends at once when it joined the top-up crowd and tapped corporate venture simultaneously. In May it pulled in a second close of its Series A, adding \$13 million to the original \$25 million. New investors were GSK's SR One, Merck Serono Ventures and Aravis SA. Not to miss out on that double, microRNA play **Miragen Therapeutics Inc.** (2008) also added to its coffers, tacking on \$4 million in June from Amgen Ventures, Broadview Ventures, and the Peierls Foundation and existing investors Atlas Venture and Boulder Ventures to its \$8 million May 2008 Series A.

There were some busy dealmakers as well. **Ensemble Discovery Corp.** (2004) inked two deals—one with **Pfizer Inc.** and one with **Bristol-Myers Squibb Co. Concert Pharmaceuticals Inc.** (2005) shored up IP on deuterated versions of pharmaceutical compounds and landed a June option-alliance on three compounds with **GlaxoSmithKline PLC**. The \$35 million Concert gained in up-front cash and equity was augmented by a \$12 million milestone in November. **Dicerna Pharmaceuticals Inc.** (2007) landed what seemed like the first RNAi deal in a very long time when it signed on **Kirin Holding Co. Ltd.'s Kyowa Hakko Kirin Co. Ltd.** division in December for a one-target oncology deal that may later get expanded. (See "Venture-Backed Dicerna Cuts First Pharma Deal as Prelude to 'B' Round," *The Pink Sheet DAILY*, January 4, 2010.) **Enlight Biosciences LLC** (2008) has doubled its stable of Big Pharma partnerships from three to six since being named to last year's A-List. Alongside **Merck & Co. Inc.**, Pfizer and **Eli Lilly & Co.** are now **Abbott Laboratories Inc.**, **Novartis AG**, and **Johnson & Johnson**. As such, the developer of next-generation discovery and development technologies has also significantly increased its cash pile, from \$39 million at last year's writing to \$78 million today.

And finally, cancer-metabolism-focused **Agios Pharmaceuticals** (2008) pulled in new management, including straight-outta-Genentech CEO David Schenkein, MD. On the scientific front, Agios scientists reported in *Nature* in December that a mutated form of a metabolic enzyme common to many brain cancers acts as an oncogene, uncovering a potential new drug target. (See "Cancer Metabolism Approach Uncovers Drug Target, Biomarker," *START-UP*, December 2009.)

Where Are They Now? Catching Up With the Classes of 2004–2008

II. Medical Devices

We wish we could pat ourselves on the back for this one, but the novelty and likely success of **Acclarent Inc.** was apparent right from the start. (See “Acclarent: Can Balloons Open Sinuses and the ENT Device Market,” *IN VIVO*, January 2006.) A member of the Series A Class of 2005, Acclarent will realize its full commercial potential as part of **Ethicon Inc.** The **Johnson & Johnson** division agreed to pay \$785 million for the ear-nose-and-throat pioneer, capping the exciting six-year run for Acclarent. The company went commercial early, obtaining FDA approval for its *Balloon Sinuplasty* device in 2005. Acclarent tried going public in 2008 but wisely withdrew the offering the next year. Instead, it raised a \$26 million Series D, bringing its total capital raised just north of \$100 million. Johnson & Johnson Development Corp. led the financing, and while CEO Bill Facteau insisted there were no strings attached to the equity financing, J&J clearly had other things in mind.

From our class of 2006, **Cardiovascular Systems Inc.**, which went public in 2008 through a reverse merger with Replidyne Inc., continued to assemble its product pipeline through external deals while pushing forward with clinical testing of its flagship *Diamondback 360* system, a minimally invasive catheter for treating peripheral arterial disease. Cardiovascular Systems signed the deals with **Ashai Intec Co. Ltd.** and **Invatec SRL**. Although Cardiovascular System’s merger with Replidyne is bearing fruit, the anticipated marriage between its 2006 classmate **Galil Medical Ltd.** and fellow ablation company **Endocare Inc.** never reached the altar. We reported on the merger as part of last year’s A-List. But the deal went sour when **HealthTronics Inc.**, a one-time suitor of Endocare, returned with a better offer leading to their merger. A court case over the matter was settled after Galil agreed to free Endocare from the merger in exchange for a \$1.75 million fee.

Several Series A selections enjoy success in the raising new funds, which is no small achievement in this market. From 2007,

the company formerly known as Innovative Metabolics, **SetPoint Medical Corp.**, secured a \$4 million Series B from investors including Series A investors Morgenthaler Ventures and Foundation Medical Partners to further develop its anti-inflammatory device, a neurostimulation implant. Acclarent 2005 classmate **Endosense SA**, developer of catheter ablation for cardiac arrhythmias, raised a €25 million (\$36 million) Series B round with Edmond de Rothschild Investment Partners leading the financing. Endosense is using the money for European commercialization and a US PMA study of its TactiCath ablation catheter.

Three companies from 2004 raised new capital. **Sadra Medical Inc.** collected a \$30 million Series C round led by Accuitive Medical Ventures. The percutaneous aortic valve replacement venture no doubt benefited from **Medtronic Inc.**’s decision to spend over \$1 billion to acquire two of Sadra’s competitors: CoreValve Inc. and **Ventor Technologies Ltd.** Medtronic or its competitors haven’t resumed shopping since the one-two punch from a year ago, but it may be only a matter of time. Meanwhile, classmate **Spinal Kinetics Inc.** secured a more modest \$5.26 million debt and equity financing to further development of its artificial spinal disc. And **CardioPolymers Inc.** wrapped up \$13 million. The former Symphony Medical is developing a biopolymer technology that would be injected in the heart to prevent atrial fibrillation.

Other companies reported forward progress that didn’t involve financing. From 2007, **Follica Inc.**, a privately held developer of novel therapies for treating baldness, hired William D. Ju, MD, as CEO. He succeeds Daphne Zohar, the PureTech Ventures investor who helped start the company. Prior to joining Follica, Ju was COO at **PTC Therapeutics Inc.** Glaucoma diagnostic device company **Sensimed AG**, meanwhile, secured a CE mark for its *Triggerfish* system, which is design to monitor continuously intraocular pressure up to 24 hours.

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