BioCentury
WEEK OF MAY 21, 2018

EUROPEAN FINANCE REPORT 2018

CHINA COMES TO EUROPE

BY STEPHEN HANSEN, ASSOCIATE EDITOR

The historically underfunded European biotech sector is in the early stages of tapping into a new stream of capital thanks to the explosion of biomedical innovation in China, which has spawned a wave of investors looking for high quality science at attractive prices.

The influx is not only welcome in a region that historically has struggled to gain the attention of U.S. investors, but could open the door to the fastest growing healthcare market in the world.

BioCentury's annual review of the European financing environment finds that European biotechs continue to tread water in the competition for capital compared to their U.S. counterparts.

As the pie has grown over the last decade, Europe's take has hovered at 20-30% of the total raised in the U.S. and Europe.

Last year, European biotechs raised $14.4 billion in public and private capital, less than one fourth of the $47.4 billion raised by U.S. companies (see "Competition for Capital").

Chinese investors are seeing that as an opportunity. All nine Chinese investors contacted by BioCentury said they're increasingly busy in Europe.

The quality of European science isn't in doubt. But for Chinese investors, it often comes at a much lower price than they find either at home or in the U.S.

"High quality science is cheaper than in the U.S.," said Sofinnova Partners' Antoine Papiernik. "With Chinese investors right now, it is more about them investing in Europe because they can see the arbitrage with the U.S. and EU."

He and other European investors said the Chinese presence is both noticeable and likely to grow.

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Alex Pasteur of F-Prime Capital, the U.S. and European successor to Fidelity Biosciences, said his firm frequently fields incoming interest from Chinese investors, noting the level "has gone up threefold or so in the last two years."

Chinese investors bring more than funding; they also have connections that can help European companies perform clinical trials and find partnering opportunities in China.

On the other hand, the path into Europe is challenging because it is fragmented and lacks the networks of Chinese that have provided access to deal flow in the U.S.

"If you're willing to spend the time, learn the landscape, I think there's less competition in Europe," said Bosun Hau of Sailing Capital in Hong Kong. "There is a lot of innovation, but one of the challenges for Chinese investors generally is that Europe is so fragmented."

"Most of our go-to contacts for industry and academia make it easier for us to tap into the U.S. network," said Kewen Jin, managing partner at Serica Capital in Shanghai. "But we definitely know and want to do a lot more in Europe."

Chinese investors have already participated in some of Europe's largest venture rounds, including a $320 million series A for T cell receptor (TCR) therapy company Immunocore Ltd., a $100 million series C for mAb platform play Kymab Group Ltd., two £100 million ($135.3 million) rounds for sequencing play Oxford Nanopore Technologies Ltd., and a $110 million series B for gene therapy company Orchard Therapeutics Ltd.

For many, the arbitrage is only the start of the story. Chinese investors are scouring Europe for opportunities with potential to compete on global markets and management teams with the ambition to do so.

ARBITRAGE OPPORTUNITY

According to Chinese investors who spoke with BioCentury, the move into Europe is directly related to the rapid expansion of the investor base in China, which has led to huge amounts of capital for investing in healthcare.

For example, according to McKinsey & Co., China-based venture or private equity funds raised $39.8 billion in 2017, nearly double the $20.2 billion raised in the prior year. Venture investments in Chinese healthcare also skyrocketed to $11.7 billion last year, more than double the $5.4 billion invested in 2016.

The flood of capital has outpaced the growth of China's innovative biotech sector, causing investors to look beyond their own borders.

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Darren Ji, founder and CEO of Elpiscience Biopharmaceuticals Co. Ltd. and venture partner of Lilly Asia Ventures, noted China's appetite for deals has saturated places like Hong Kong and Shanghai with healthcare investors. "If you throw one rock in Shanghai you hit three people, and two are investors — one of whom is in life sciences," he told BioCentury.

According to Sailing's Hau, that has escalated valuations of local biotechs.

"I think the Chinese valuations are just astronomical," said Hau, whose firm invests in technology and consumer plays as well as healthcare. "That is forcing the Chinese investors who have the ability to invest overseas, who have outside capital — they are looking for more attractively priced assets."

ORI Capital's Simone Song agreed, labeling as "two different animals" the valuations between Europe and China. "One is very sensible and the other is extremely not sensible. That explains why I don't have one China-based company in our portfolio. I would love to be in a Chinese company, but I have just not found the right deal."

Song, whose Hong Kong fund aims to find disruptive technologies spanning the healthcare space, including immuno-oncology and artificial intelligence, thinks there are three primary drivers for the disparity.

First, she said, "China has printed too much money, so there's hot money chasing something they don't understand." Second, it is simple supply and demand. "There is not an ample supply of good companies," she said.

The third reason is a misconception about what a company's valuation really means. "The popular myth is the higher the valuation is, the better the company is," Song said.

Ally Bridge's Frank Yu noted each region represents a different valuation tier. "Chinese companies tend to have a hefty China premium, and the U.S. on the venture side is lower. And then the bottom is European assets."

The arbitrage extends to public companies. "The European-U.S. arbitrage opportunity is a major driver of our investment gains," said Yu. For example, the Hong Kong firm invested in CAR T company Cellectis S.A. prior to its NASDAQ listing in 2015. At the end of 2014, Cellectis' market cap was $438.5 million on Euronext. Three months later the company raised $228.3 million in a follow-on on NASDAQ that gave it a postmoney valuation above $1.4 billion.

"Our European-U.S. arbitrage has been pretty much consistently 2x within several months," Yu said.

Other European investments in Ally Bridge's portfolio include T cell therapy play Adaptimmune Therapeutics plc, antibiotics company Nabriva Therapeutics plc, and Swiss specialty pharma Vifor Pharma Ltd.

About one-quarter of the European biotechs that listed on NASDAQ since 2012 had at least doubled in market cap by the end of 1Q18 compared with their postmoney valuation, and more than half saw at least a 25% increase (see "Europeans on NASDAQ").

European companies that first listed in Europe and then raised money on NASDAQ also enjoyed a step up.

Out of 23 European biotechs that completed a NASDAQ follow-on since 2012, 14 (61%) are in the black, and 11 (48%) are up more than 50% from the time of their listing to the end of 1Q18.

Neurology play GW Pharmaceuticals plc tops the list, having first listed on the London Stock Exchange in 2001. In 2013, it listed on NASDAQ with a postmoney valuation of $131.4 million. The biotech has since

COMPETITION FOR CAPITAL

In 2017, Europe's share of the total of public and private capital raised in the U.S. and Europe was 23% , in line with the prior decade where Europe's cut averaged about 21%. But the size of the capital pie has increased substantially. During the five year period 2013-17, the annual total amount averaged $54.9 billion, more than double the previous five years' annual average of $26.8 billion from 2008-12. Data includes both public and private financings, including debt. Financings for companies that inverted are included in the region of domicile at the time of the offering. *Source: BCIQ: BioCentury Online Intelligence*

raised nearly $1.1 billion in capital and as of May 3 had a market cap of $4.4 billion.

In another case, antibody play argenx S.E. went public in 2014 on Euronext and then last year raised $114.7 million on NASDAQ at a postmoney valuation of $456.8 million. argenx has since gained 566% to $3 billion.

However, several investors said it's not all upside on the venture side — the highest profile European venture deals often come at a premium compared to the U.S. due to scarcity value.

"The deals that are higher profile, higher quality, that everyone knows about, I think actually the valuations in my view tend to be higher in Europe on a relative basis than the U.S.," Hau said.

WANTED: AMBITION AND INNOVATION

For some Chinese investors, the driving force in Europe is more access to innovation than the valuation arbitrage.

According to Hillhouse Capital's Ting Jia, Europe's lower valuations are a nice add-on, but his firm's main motivation is to find innovation.

"Europe is a region we want to spend more time in" because of the opportunity to find really innovative assets and help them grow. "I think Europe has a very parallel level of innovation compared to the U.S.," he said.

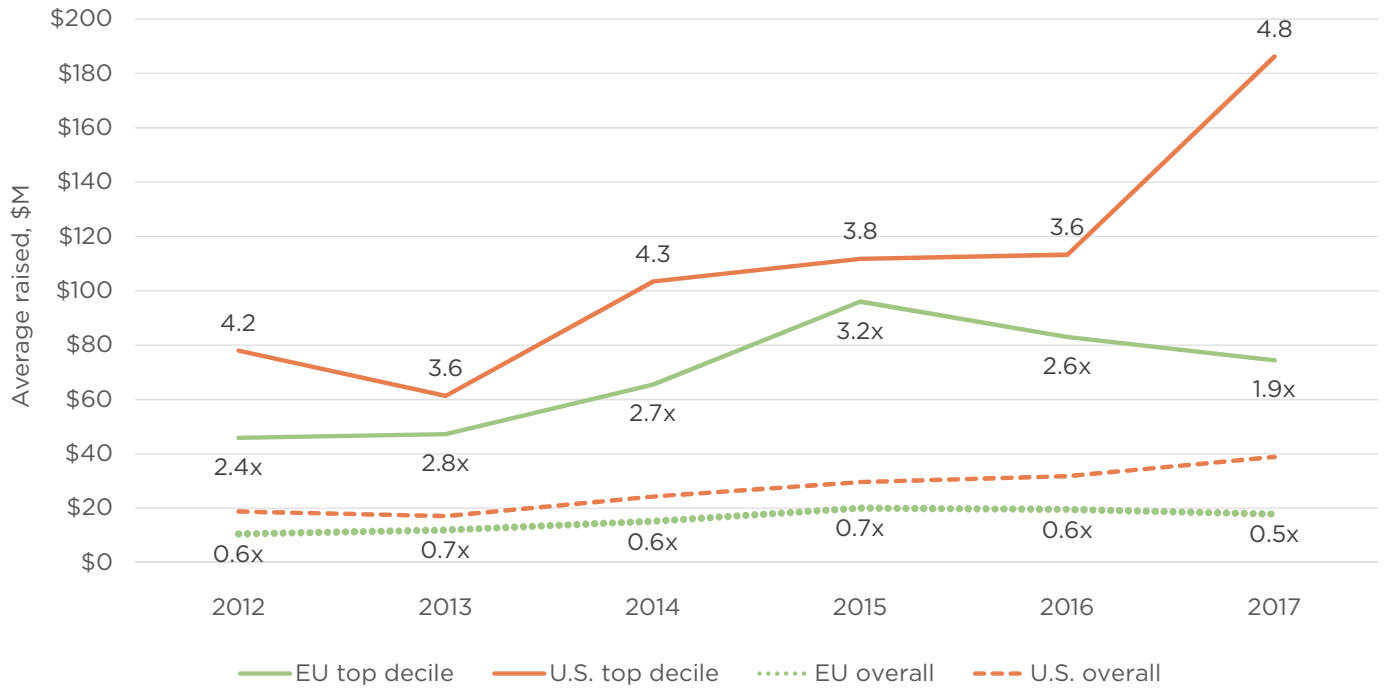
Hillhouse, based in Beijing, invests across the healthcare, internet, tech and consumer spaces. The firm participated in its first European biotech venture financing in December as part of the €50 million ($59.6 million) series C round for vaccines play Hookipa Biotech AG last December.

F-Prime's Pasteur said he is finding that Chinese investors are looking for innovation that is world-class. "Rather than just more local propositions that might be good investments at a local level, they want to take back something that is high gloss and impressive," he told BioCentury.

According to Jia, that means looking at the company leadership. "The one part is innovation. But the second is the management team has to have

CAPITAL RATIONING

In 2017, the top tier of private European biotechs continued to raise enough capital to be globally competitive. The top decile of private European companies averaged $74.3 million per round, nearly double the overall U.S. average of $38.8 million. However, the top capital magnets in Europe still trail well behind the top decile of private U.S. biotechs, which raised on average $186.2 million last year. And the gap between the best of Europe and U.S. continues to grow, as in 2017 the top decile of U.S. biotechs fundraisers averaged 150% more than their European counterparts, up from the 37% gap in 2016. The top U.S. decile in 2017 was buoyed by eight offerings of $200 million or more, led by circulating tumor DNA diagnostic company **Grail Inc.** which raised in $900 million in a series B round. Europe had only one $200 million offering in 2017, by **ADC Therapeutics S.A.** The numbers for each year refer to the multiples compared with the U.S. average. Tranches within a round are counted in the year each tranche closed. Analysis includes venture debt but excludes private holding company **Roivant Sciences GmbH**. *Source: BCIQ: BioCentury Online Intelligence*



the ambition or the capability to drive the company over the longer term to be a multi-billion dollar company, rather than a multi-hundred million dollar company," he said.

Ally Bridge also prioritizes that kind of ambition. "We focus on European life science assets with strong U.S. aspirations and capabilities," Yu said.

Most of the investors said it is too early to identify clear trends in the types of assets Chinese investors are hunting. But some described interest in cell therapy and gene therapy companies, areas that are also of high interest in China domestically (see BioCentury Innovations, May 17, 2018).

Hau and Syncona Ltd.'s CEO Martin Murphy noted there's increased interest from Chinese investors in big data, including technologies centered on artificial intelligence and genomics.

Syncona, the listed venture investment fund based in London, has been focusing on investments in cell and gene therapies, areas China has also prioritized.

MORE IS NOT ENOUGH

The influx of Chinese investors could go some way to lessening the shortfall in funding in Europe. But they are not alone in noticing the opportunity.

European biotech appears to be accessing more international capital. In addition to Asian money, interest from U.S. VCs continues to grow. In 2017, each of the 10 largest venture rounds raised in Europe had at least one U.S. investor; three also included a Chinese investor (see "U.S. Investments in Top Rounds").

The offshore investors will be bolstering several pan-European VCs that are deploying large new funds. In February, Andera Partners (formerly

U.S. INVESTMENTS IN TOP ROUNDS

In 2017, all of the top 10 venture rounds in Europe had at least one U.S.-based investor, with three biotechs — gene therapy play **Orchard Therapeutics Ltd.**, antibiotics company **Iterum Therapeutics Ltd.** and vaccines play **Hookipa Biotech AG** — also attracting investment from Asia. U.S. investors shown in bold. VC firms were assigned to a country based on the location of their headquarters. (A) Pivotal bioVenture, while based in the U.S., is solely funded by **Nan Fung Group** of Hong Kong; (B) InflaRx GmbH prior to IPO in November 2017; *Source: BCIQ: BioCentury Online Intelligence*

Company	Raised	Round	Investors	Technology	Disease area
ADC Therapeutics S.A. (Switzerland)	$200.0	Undisclosed	**Redmile Group**, AstraZeneca plc, **Auven Therapeutics Management**, Wild Family Office	Antibody-drug conjugates	Cancer
Orchard Therapeutics Ltd. (U.K.)	$110.0	Series B	Temasek, **F-Prime Capital**, **RTW Investments**, Pavilion Capital, Baillie Gifford, UCL Technology Fund, **Cowen Healthcare Investments**, **Agent Capital**, ORI Capital, Juda Capital, 4BIO Capital	Gene therapy	Inherited rare diseases
Autolus Ltd. (U.K.)	$80.0	Series C	Nextech Invest, Syncona Partners LLP, Woodford Investment Management, **Cormorant Asset Management**, Arix Bioscience	T cell therapies	Cancer
Cell Medica Ltd. (U.K.)	$73.3	Series C	**Invesco**, Woodford Investment Management, Touchstone Innovations plc	T cell therapies	Cancer and infectious diseases
Iterum Therapeutics Ltd. (Ireland)	$65.0	Series B	**Domain Associates**, **Bay City Capital**, **Sofinnova Ventures**, **Canaan Partners**, **Frazier Healthcare**, **New Leaf Venture Partners**, Advent Life Sciences, Arix Bioscience plc, Pivotal bioVenture (A)	Antibiotics	Bacterial infections
Hookipa Biotech AG (Austria)	$59.6	Series C	Sofinnova Partners, Hillhouse Capital, **Takeda Ventures**, HBM Partners, Forbion Capital Partners, BioMedPartners, Boehringer Ingelheim Venture Fund, Sirona Capital, **Gilead Sciences Inc.**	Therapeutic vaccines	Cancer and infectious diseases
Immatics Biotechnologies GmbH (Germany)	$58.0	Series E	Wellington Partners, dievini Hopp BioTech, AT Impf GmbH, **Amgen Inc.**	T cell therapies and bispecific antibodies	Cancer
InflaRx N.V. (NASDAQ:IFRX) (Germany) (B)	$55.0	Series D	**Bain Capital**, **RA Capital Management**, **Cormorant Asset Management**	mAbs	Autoimmune and inflammatory diseases
Bicycle Therapeutics Ltd. (U.K.)	$51.3	Series B	**Atlas Venture**, Novartis Venture Fund, **SR One**, **SV Life Sciences**, **Longwood Fund**, Cambridge Innovation Capital, **Vertex Ventures HC**	Bicyclic peptides	Cancer
Nouscom AG (Switzerland)	$48.7	Series B	Abingworth Management, **Versant Ventures**, LSP, **5AM Ventures**	Neoantigen vaccines and oncolytic viruses	Cancer

"IF YOU THROW ONE ROCK IN SHANGHAI YOU HIT THREE PEOPLE, AND TWO ARE INVESTORS — ONE OF WHOM IS IN LIFE SCIENCES."

DARREN JI, ELPISCIENCE BIOPHARMACEUTICALS CO. LTD.

Edmond de Rothschild Investment Partners) closed its BioDiscovery 5 fund at €345 million ($428 million).

Fresh local capital includes the $400 million SV Health Investors Fund VI, which closed in April 2017. And Sofinnova Partners has raised nearly $700 million in the last two-and-a-half years across two funds: Sofinnova Capital VIII at €300 million ($324.6 million) in December 2015, and Sofinnova Crossover I at €275 million ($340.5 million), which closed in April.

Sofinnova's crossover vehicle, along with the $300 million crossover fund raised by Medicxi in 2017, will help European biotechs cross the bridge to the public markets, which in Europe have become more receptive to biotech stories.

In 2017, 126 European companies raised on average $64.7 million in the public equity markets, bouncing back from 2016's average of $39.2 million by 106 companies (see "Public Financings 2012-17").

Also, the 126 fundraisers mark the largest number of European biotechs tapping the public markets since BioCentury began tracking financings in 1994.

The top 20 European fundraisers each have attracted $200 million or more since 2011 (see "Public Capital Magnets").

For private funding, the most favored European companies are raising money at a level that's globally competitive. In 2017, the top decile of European fundraisers averaged $74.3 million, nearly double the U.S. overall average of $38.8 million (see "Capital Rationing").

Nevertheless, European VCs contend there's still not enough money to fund all of the best scientific ideas coming out of Europe.

Forbion Capital's Sander Slootweg told BioCentury his firm sees more than 700 deals annually, but only invests in four to five — with many more that he considers to be "investment grade" but has to pass on.

"We are definitely seeing more quality deals than we can or will invest in," Slootweg said.

All eight European VCs contacted by BioCentury thought the inflows from Chinese or Asian funds will be positive for the sector.

"The market is still underserved, so if we see fresh capital coming to Europe from U.S. investors — in many instances they like to team up with a leading local VC like us — then I think on balance it is a plus. The same would apply to Asian capital," said Slootweg.

The local investors also thought it unlikely the Chinese money would crowd out European VCs. "They'd have to divert a lot of their money from the U.S. to Europe to create that kind of competition," said Andera Partners' Raphaël Wisniewski.

Instead, U.S. and European VCs thought Chinese investors would facilitate access to regulatory bodies, top hospitals and CROs in China

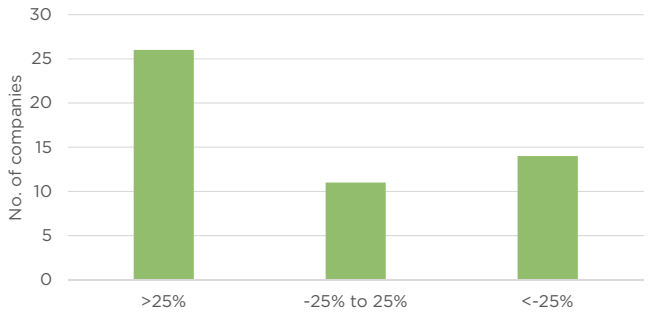
EUROPEANS ON NASDAQ

At least 51 European biotechs have raised money on NASDAQ since 2012, and more than half have added at least 25% in market cap since joining the exchange, whether via an IPO or a follow-on.

Galapagos N.V. (Euronext:GLPG; NASDAQ:GLPG) was the most valuable member of the group at more than $5 billion in market cap at the end of 1Q18. It listed on NASDAQ in 2015 after 10 years on Euronext.

Not all European bellwethers have gone for NASDAQ -- **Genmab A/S** (CSE:GEN) remains listed only in Copenhagen. And Actelion Ltd. maintained its listing only in Switzerland prior to its takeout by **Johnson & Johnson** (NYSE:JNJ)

Market cap changes based on closing prices at the end of 1Q18. *Source: BCIQ: BioCentury Online Intelligence*



to facilitate global development and access to the Chinese market long-term.

For instance, Hau noted that because Sailing Capital's main LP is the Shanghai municipal government, the firm can add to shareholder value through "unique relationships that extend all the way up to the highest levels of government," including heads of the State Drug Administration (formerly CFDA), the Ministry of Health and Ministry of Science.

EUROPEAN HURDLES

While the Chinese investors intend to invest more in Europe, they acknowledged there are obstacles.

"There are opportunities if you're willing to do the work and get connected," Hau said. "It just takes more work. But you can find good deals in Europe that you otherwise could not find in the U.S., and definitely not in China."

Unlike the U.S. hubs in Boston and the San Francisco Bay Area, the pockets of innovation in Europe are not only more dispersed, but are being developed within different cultural contexts that can have nuanced legal differences.

"Europe is not one country, as we know," Slootweg said. "Doing a deal under French law, to participate in a French board dinner where all the decisions get taken, that could be quite difficult to immediately adjust and adapt to."

Sofinnova's Papiernik agreed that while it is culturally easier to adapt to the U.S., over time the same should be true for China.

Investors from both regions will also have to work harder to establish relationships, because with fewer Chinese network connections in Europe than in the U.S., Chinese investors have fewer natural contact points to get into deal flow.

"Look at investments in the U.S. by Chinese VCs. Quite often the founder or major team members are Chinese," C-Bridge's Sean Cao said. "Very few of them have gone to Europe. That's probably why you haven't seen as many of those investments in Europe, because when you don't know anybody, that makes it harder."

EUROPEAN VENTURE ROUNDS WITH CHINESE INVESTORS

At least nine European companies raised venture rounds with Chinese investors in 2017. Three of the rounds were in Europe's top 10 largest of the year. Several drew other ex-European investors as well, with the largest round, from **Orchard Therapeutics Ltd.**, drawing investments from Singapore-based Temasek and multiple U.S. VCs. Chinese investors are shown in bold. VC firms were assigned to a country based on the location of their headquarters. (A) Pivotal bioVenture, while based in the U.S., is solely funded by **Nan Fung Group** of Hong Kong; (B) In December 2017, Eloxx Pharmaceuticals Ltd. reverse-merged with Sevion Therapeutics, Inc. to form **Eloxx Pharmaceuticals Inc.** (NASDAQ:ELOX), which is based in the U.S. but maintains R&D operations in Israel; *Source: BCIQ: BioCentury Online Intelligence*

Company	Raised	Round	Investors	Technology	Disease area
Orchard Therapeutics Ltd. (U.K.)	$110.0	Series B	Temasek, F-Prime Capital, RTW Investments, Pavilion Capital, Baillie Gifford, UCL Technology Fund, Cowen Healthcare Investments, Agent Capital, **ORI Capital, Juda Capital,** 4BIO Capital	Gene therapy	Inherited rare diseases
Iterum Therapeutics Ltd. (Ireland)	$65.0	Series B	Domain Associates, Bay City Capital, Sofinnova Ventures, Canaan Partners, Frazier Healthcare, New Leaf Venture Partners, Advent Life Sciences, Arix Bioscience plc, **Pivotal bioVenture** (A)	Antibiotics	Bacterial infections
Hookipa Biotech AG (Austria)	$59.6	Series C	Sofinnova Partners, **Hillhouse Capital**, Takeda Ventures Inc., HBM Partners, Forbion Capital Partners, BioMedPartners, Boehringer Ingelheim Venture Fund, Sirona Capital, Gilead Sciences Inc.	Therapeutic vaccines	Cancer and infectious diseases
Gamida Cell Ltd. (Israel)	$40.0	Undisclosed	Clal Biotechnology Industries, Novartis AG, Israel Healthcare Ventures, Shavit Capital, Israel Biotech Fund, **VMS Investment Group**	Cell therapy	Hematological diseases, including cancer
Eloxx Pharmaceuticals Ltd. (Israel) (B)	$38.0	Series C	Catalyst Ventures, LSP, Pontifax, Korea Investment Partners, DSC Investment, Quark Venture, **GF Securities**	Small molecules	Rare diseases with nonsense mutations
Atlas Genetics Ltd. (U.K.)	$35.0	Series D	Johnson & Johnson Development Corp., BB Biotech Ventures, LSP, Novartis Venture Fund, Consort Medical plc, RMI Partners, **Wondfo Biotech**, Technology Venture Partners	Diagnostics	Infectious diseases
Biosceptre International Ltd. (U.K.)	$10.7	Series A	**Tuspark Science and Technology Service Group**	Non-functioning P2RX7 receptor targeting platform	Cancer
Congenica Ltd. (U.K.)	$9.9	Series B	Amadeus Capital Partners, Cambridge Innovation Capital, Parkwalk Advisors, **Healthlink Capital, BGI Genomics Co. Ltd.**, Future Planet Capital	Genome analysis software	Genomics
HiberGene Diagnostics Ltd. (Ireland)	$7.1	Series B	Kernel Capital, Cantor Fitzgerald, **Medcaptain Medical Technology Co. Ltd.**	Diagnostics	Infectious diseases

Serica's Jin said a starting point is to establish good relationships with the major local VCs, who can not only introduce investors to deals but be trusted managers of the portfolio companies.

"We feel we need to find people who are based in Europe and very knowledgeable and maybe co-invest with some European VCs," he said. "In addition, work with some serial entrepreneurs who are based in Europe. We are very active and that's our plan for the second fund."

NETWORKING BENEFITS

The networks Chinese investors have started to develop are bearing fruit.

In 2017, at least 10 European biotechs raised venture rounds that included Chinese investors, three of which were in the top 10 for money raised that year and are among Europe's venture capital magnets (see "European Venture Rounds with Chinese Investors" and "Venture Capital Magnets").

ORI Capital co-led two of the big deals in the past two years.

In November 2016, the firm co-led Kymab's $100 million series C round alongside Shenzhen Hepalink Pharmaceutical Co. Ltd.

Song said she had been aware of Kymab's work and that of its scientific founder and CSO Allan Bradley through connections between Bradley's and her scientific network. Song said ORI invested because of the best-in-class potential of Kymab's transgenic mouse platform, and its immuno-oncology focus.

Kymab CEO David Chiswell told BioCentury that having the Chinese investors on board has educated the company on clinical development and regulatory changes in China, which could help unlock future value.

According to F-Prime's Pasteur, his connection to ORI through the Fidelity China network laid the groundwork for ORI's Orchard investment.

In 2016, Orchard raised $30.7 million in a series A round from founding investors F-Prime and the UCL Technology Fund.

In December, ORI and Baillie Gifford co-led Orchard's $110 million series B round. Other investors included Singapore-based Temasek, China-based Juda Capital along with U.S. firms Cowen Healthcare Investments, Pavilion Capital, RTW Investments, Agent Capital and 4BIO Capital.

Song said ORI had been scanning for new gene therapy plays and was impressed by the results. "For Orchard, the data is so impressive because it is a cure," she said.

At the time of the investment, Orchard's most advanced program was OTL-101, a gene therapy that comprises autologous $CD34^+$ hematopoietic stem cells transduced *ex vivo* with an EFS lentiviral vector encoding the ADA gene. Early data from a Phase I/II trial showed 100% overall survival in 32 patients with adenosine deaminase severe combined immunodeficiency (ADA-SCID).

In an April deal with GlaxoSmithKline plc, Orchard gained the pharma's rare disease gene therapy portfolio, which includes the marketed ADA-

VENTURE CAPITAL MAGNETS

Of Europe's top 20 venture fundraisers, five have attracted private capital from Chinese investors: sequencing play **Oxford Nanopore Technologies Ltd.**, immuno-oncology company **Immunocore Ltd.**, mAb platform play **Kymab Group Ltd.**, gene therapy company **Orchard Therapeutics Ltd**., and antibiotics play **Iterum Therapeutics Ltd.** The table includes therapeutics and genomics companies and excludes diagnostics, tools, supply/service and generics companies. The table also excludes **Roivant Sciences GmbH**, a holding company that finances subsidiaries and has raised $1.7 billion. Figures for companies that have gone public include only private money raised: (A) Oxford Nanopore raised an additional $139.2 million in March 2018; (B) Gene editing company **CRISPR Therapeutics AG** (NASDAQ:CRSP) went public and raised $97 million in October 2016, and sold a $130.8 million follow-on earlier this year; (C) T cell therapy play **Adaptimmune Therapeutics plc** (NASDAQ:ADAP) sold a $191.3 million IPO in May 2015 and raised a further $107.9 million in two offerings last year; (D) Rare disease and specialty products in-licensor **Mereo BioPharma Group plc** (LSE:MPH) raised $16.4 million in an IPO in June 2016 and $18.8 million in a placing last year; (E) **Nighstar Therapeutics plc** (NASDAQ:NITE), formerly NightstaRx Ltd., raised $86.3 million in an IPO in September 2017; $M; *Source: BCIQ: BioCentury Online Intelligence*

Company	2011-17 raised $M	Last venture financing
Oxford Nanopore Technologies Ltd.	$450.5 (A)	12/12/16
ADC Therapeutics S.A.	$435.0	10/23/17
CureVac AG	$320.5	11/8/16
Immunocore Ltd.	$320.0	7/16/15
Symphogen A/S	$199.5	10/22/15
CRISPR Therapeutics AG (NASDAQ:CRSP) (B)	$198.5	6/24/16
Kymab Group Ltd.	$190.0	11/24/16
Autolus Ltd.	$180.9	9/26/17
Cell Medica Ltd.	$178.1	3/16/17
DalCor Pharma U.K. Ltd.	$150.0	4/19/16
Novimmune S.A.	$143.0	5/11/16
Orchard Therapeutics Ltd.	$140.7	12/20/17
Adaptimmune Therapeutics plc (NASDAQ:ADAP) (C)	$130.0	9/25/14
Mission Therapeutics Ltd.	$127.9	2/2/16
Mereo BioPharma Group plc (LSE:MPH) (D)	$118.6	7/29/15
Cardiorentis AG	$118.3	1/11/16
Nightstar Therapeutics plc (NASDAQ:NITE) (E)	$107.3	6/29/17
Iterum Therapeutics Ltd.	$105.0	5/19/17
immatics biotechnologies GmbH	$104.3	10/4/17
F2G Ltd.	$102.0	6/20/16

SCID gene therapy Strimvelis. GSK received a 19.9% stake in the biotech in return.

For Chinese pharma Fosun International Ltd., partnering with U.K. investor Arix Bioscience plc has helped it navigate the European investment environment.

In their November deal, Fosun became an LP and gained the potential to license technologies from Arix's portfolio companies and co-invest in future deals.

Arix's Ed Rayner said the deal goes beyond just investing in future portfolio companies or helping them expand into China. He said over the longer-term, Arix hopes to get a reciprocal benefit from Fosun's network.

"With the help of Fosun, we'd like to look at what innovation is happening in China," Rayner said.

Chinese investors also tapped European connections to participate in one of Europe's largest venture rounds of 2018 — Crescendo Biologics Ltd.'s $70 million series B round, which was led by Andera and included fellow new investor Quan Capital, which has set up shop in Shanghai and San Francisco.

PUBLIC CAPITAL MAGNETS

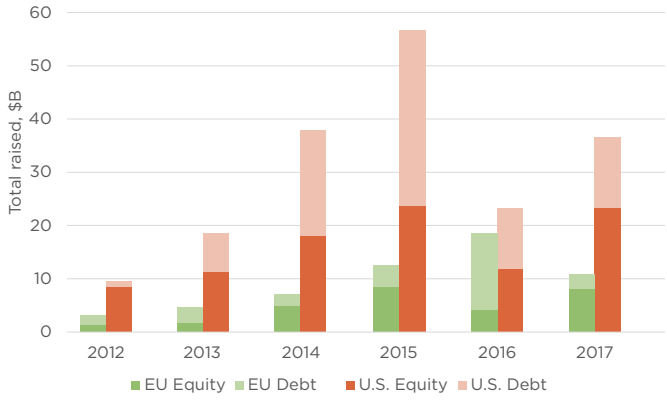
European companies have steadily increased the amount of public equity raised, with many in the top tier raising large sums from U.S. investors. Of the top 20 fundraisers since 2011, 14 have a primary or secondary listing on NASDAQ. The analysis includes the top 20 fundraisers among therapeutics companies and excludes diagnostics, tools, supply/service and generics companies. It also excludes legacy therapeutics companies founded prior to 1980, as well as inverters. Debt offerings are included. (A) Total raised includes any private financings completed in 2011-17; *Source: BCIQ: BioCentury Online Intelligence*

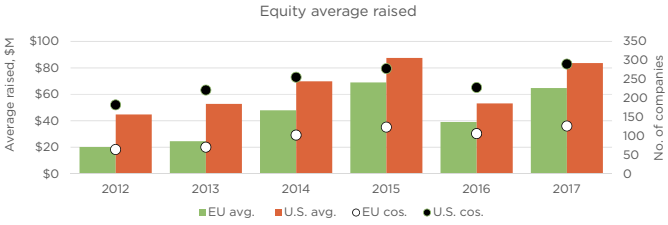
Company	2011-17 public raised, $M	2011-17 total raised, $M (A)
GW Pharmaceuticals plc (NASDAQ:GWPH)	$1,073.4	$1,073.4
Galapagos N.V. (Euronext:GLPG; NASDAQ:GLPG)	$807.3	$807.3
Circassia Pharmaceuticals plc (LSE:CIR)	$757.5	$855.1
Prothena Corp. plc (NASDAQ:PRTA)	$595.4	$595.4
Axovant Sciences Ltd. (NASDAQ:AXON)	$561.0	$561.0
Ablynx N.V. (Euronext:ABLX; NASDAQ:ABLX)	$539.3	$539.3
argenx S.E. (Euronext:ARGX; NASDAQ:ARGX)	$487.9	$531.3
Genfit S.A. (Euronext:GNFT)	$484.9	$484.9
DBV Technologies S.A. (Euronext:DBV; NASDAQ:DBVT)	$468.4	$468.4
Pharming Group N.V. (Euronext:PHARM)	$414.7	$414.7
Ascendis Pharma A/S (NASDAQ:ASND)	$399.3	$459.3
Cellectis S.A. (Euronext:ALCLS; NASDAQ:CLLS)	$341.6	$341.6
Erytech Pharma S.A. (Euronext:ERYP; NASDAQ:ERYP)	$316.5	$316.5
Adaptimmune Therapeutics plc (NASDAQ:ADAP)	$299.2	$429.2
uniQure N.V. (NASDAQ:QURE)	$281.6	$327.9
Bavarian Nordic A/S (CSE:BAVA)	$270.3	$270.3
MorphoSys AG (Xetra:MOR; NASDAQ:MOR)	$236.7	$236.7
Genmab A/S (CSE:GEN)	$222.1	$222.1
Forward Pharma A/S (NASDAQ:FWP)	$220.5	$220.5
Swedish Orphan Biovitrum AB (SSE:SOBI)	$219.8	$219.8

PUBLIC FINANCINGS 2012-17

More European public biotechs raised money in 2017 — 126 companies — than BioCentury has recorded since it started tracking financings in 1994 (lower chart, circles). The 126 averaged $64.7 million in equity deals, bouncing back from a four-year low in 2016, which averaged $39.2 million. The change mirrored the U.S. average, which also bounced back in 2017 from a four-year low in 2016.

Overall, public European biotechs raised $8.2 billion in equity financings, roughly one-third of the $24.3 billion raised by their U.S. counterparts. Totals below include equity and debt; averages are equity only. *Source: BCIQ: BioCentury Online Intelligence*





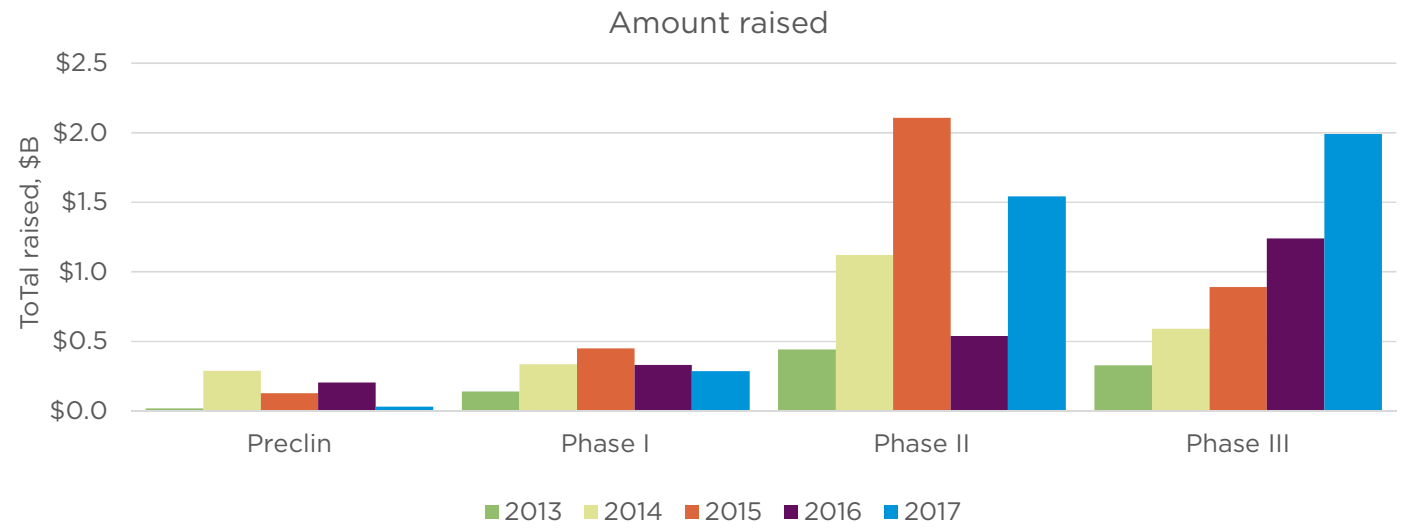
PUBLIC FINANCINGS BY STAGE

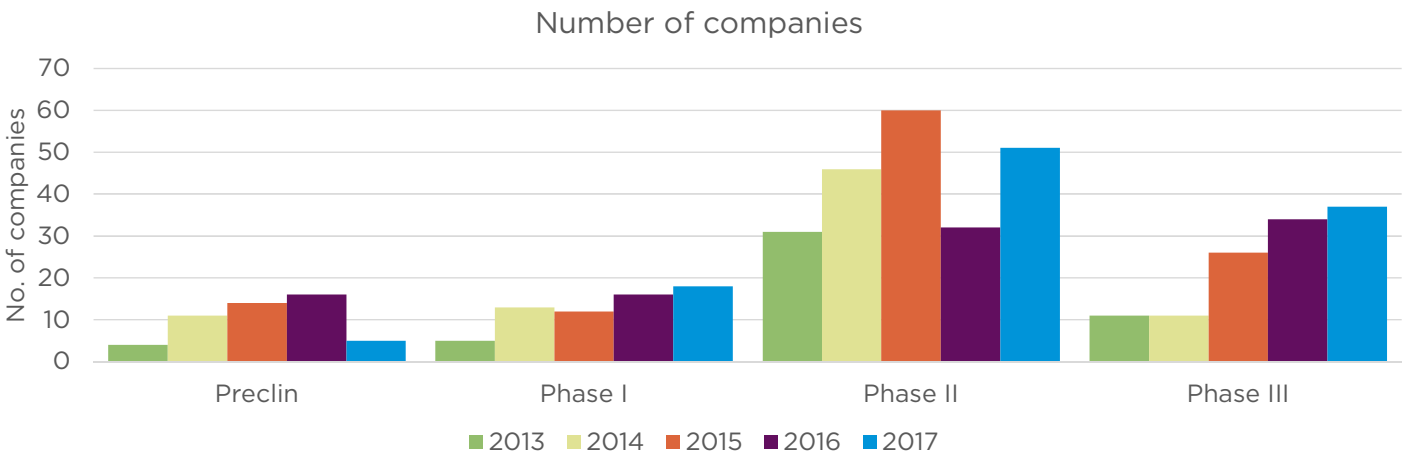
European public companies in Phase III have increasingly tapped the capital markets over the last five years, with 2017 marking the high point at nearly $2 billion in new money at an average of $53.8 million per round.

Public biotechs in Phase II showed the largest year-over-year gains, both in the number of companies raising money and in the amount collected per round; 19 more companies raised over $1 billion more than in 2016, and nearly doubled the average Phase II public financing round to $30.8 million.

The averages for preclinical or Phase I biotechs didn't change, although fewer preclinical companies raised money than in the prior three years.

Companies in Phase I/II at the time of financing are grouped with Phase I; Phase II/III companies are grouped with Phase II. The data exclude companies that did not disclose the phase of their lead product at the time of the financing and companies not developing therapeutics. *Source: BCIQ: BioCentury Online Intelligence*



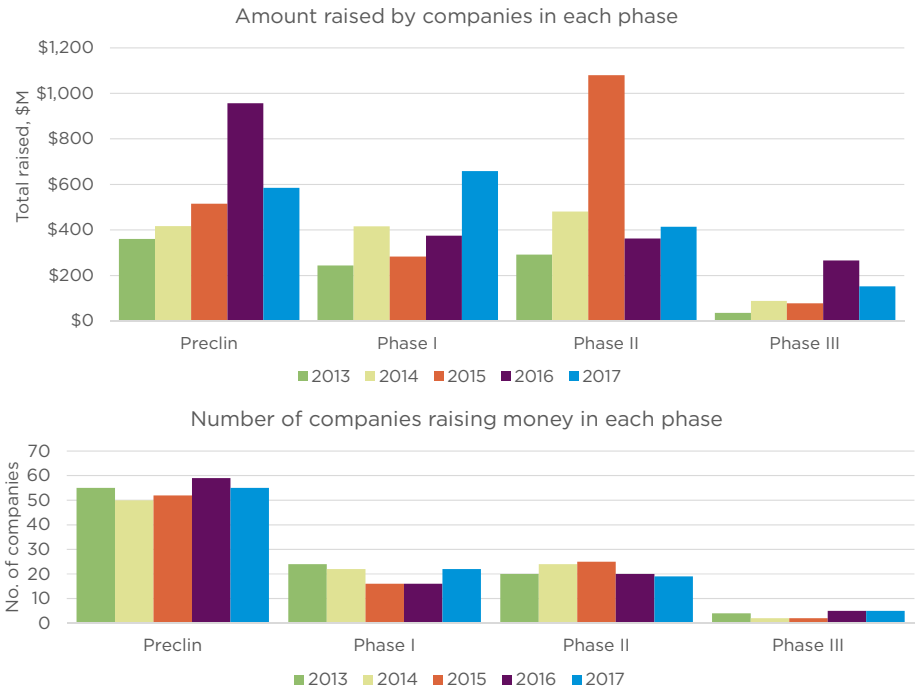


PRIVATE FINANCINGS BY STAGE

For the first time in the past five years, private European biotechs in Phase I set the high watermark for total money raised. In 2017, 22 Phase 1 companies raised $658.9 million, up 76% from $374.1 million raised by 16 companies in 2016. Each company raised $30 million on average in 2017, up 28% from $23.4 million in 2016. The jump was driven by a $200 million undisclosed venture round by **ADC Therapeutics S.A.** and a $110 million A round by gene therapy play **Orchard Therapeutics Ltd.**

Phase III companies, while down from last year's high of $266.3 million to $152.4 million in 2017, continued an upward trend over the last five years. The number of Phase III companies raising money is still in the low single digits. Preclinical companies saw the largest drop in capital raised from $956.6 million in 2016 to $584.7 million last year, although the 2016 figure was driven by several financings over $100 million, including **CRISPR Therapeutics AG** (NASDAQ:CRSP) and **Kymab Group Ltd.**

In the chart below, tranches are recorded in the year the funds were received. Companies in Phase I/II at the time of financing are grouped with Phase I; Phase II/III companies are grouped with Phase II. The data exclude companies that did not disclose the phase of their lead product at the time of the financing, companies not developing therapeutics, and private holding company **Roivant Sciences GmbH**. *Source: BCIQ: BioCentury Online Intelligence*



According to Crescendo CEO Peter Pack and Quan's Marietta Wu, the introduction was made through existing investor Sofinnova Partners. Pack told BioCentury that following an initial meeting in January, Quan was able to efficiently complete the due diligence and pushed for the deal to close quickly. "They were really impressive because they knew exactly what to ask. They were really well informed," he said.

Like other Chinese VCs, Quan is looking for high quality innovation regardless of geography. Wu said Quan bought into Crescendo because of the biotech's experienced management team, Humabody mAb platform with high differentiation potential, and innovative programs. bc

COMPANIES AND INSTITUTIONS MENTIONED

Adaptimmune Therapeutics plc (NASDAQ:ADAP), Abingdon, U.K.
argenx S.E. (Euronext:ARGX; NASDAQ:ARGX), Breda, the Netherlands
Arix Bioscience plc (LSE:ARIX), London, U.K.
Cellectis S.A. (Euronext:ALCLS; NASDAQ:CLLS), Paris, France
Crescendo Biologics Ltd., Cambridge, U.K.
Elpiscience Biopharmaceuticals Co. Ltd., Shanghai, China
Fosun International Ltd. (HKSE:656), Shanghai, China
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
GW Pharmaceuticals plc (NASDAQ:GWPH), Cambridge, U.K.
Hookipa Biotech AG, Vienna, Austria
Immunocore Ltd., Abingdon, U.K.
Kymab Group Ltd., Cambridge, U.K.
Nabriva Therapeutics plc (NASDAQ:NBRV), Dublin, Ireland
Orchard Therapeutics Ltd., London, U.K.
Oxford Nanopore Technologies Ltd., Oxford, U.K.
Shenzhen Hepalink Pharmaceutical Co. Ltd. (SZSE:002399), Shenzhen, China
State Drug Administration (SDA), Beijing, China
Syncona Ltd. (LSE:SYNC), London, U.K.
Vifor Pharma Ltd. (SIX:VIFN), Glattbrugg, Switzerland

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McKinsey & Co. "Building bridges to innovation." (2017)
Romeo, M. "Orchard's supply." *BioCentury* (2017)

EMERGING COMPANY PROFILE

ACCENT ON RNA

BY JAIME DE LEÓN, STAFF WRITER

With its debut Friday with a $40 series A, Accent Therapeutics Inc. became the second disclosed newco to jump into the nascent arena of RNA epigenetics. The biotech has identified enzymes it believes drive cancer by modifying RNA, rather than DNA, to alter gene expression. It plans to target the enzymes with small molecules.

DNA- and histone-modifying enzymes, such as histone deacetylases (HDACs), have long been targeted by drug companies based on their role in creating patterns of gene expression that underlie disease. At least five small molecule HDAC inhibitors are marketed for cancer. But humans also produce RNA-modifying enzymes, roughly 140 of them. Most of those also control gene expression, yet the class has not been on the radar of therapeutics companies.

According to Accent President and CSO Robert Copeland, recent studies have linked specific RNA-modifying enzymes to diseases, suggesting the protein class stands to expand the universe of druggable targets.

"I felt, looking at the space, that there would be many targets that would be druggable by small molecule inhibitors," Copeland told BioCentury.

He said Accent was largely the brainchild of the The Column Group's Larry Lasky, who took an interest in RNA epigenetics — also referred to as epitranscriptomics — and brought Copeland together with Accent's academic founders: Stanford University Professor Howard Chang and University of Chicago Professor Chuan He. Both are leaders in the field.

The Column Group and Atlas Venture jointly led Accent's series A, with participation from EcoR1 Capital. Lasky and Atlas' Jason Rhodes have seats on the biotech's board.

In collaboration with Chang and He, Accent analyzed over 300 cancer cell lines and identified 60 modifications in over 600 transcripts that are more or less frequent than in healthy cells. To identify which of those transcripts promote proliferation of cancer cells, the group used a combination of bioinformatics, chemical biology and a CRISPR-cas9 (CRISPR-associated protein 9) screen to knock out the genes that encode the transcripts.

The results pointed to 19 known RNA-modifying enzymes that the company considers high-value targets for cancer drug development.

Accent has whittled that list down to four undisclosed enzymes for which it is actively developing small molecule inhibitors. Copeland said the enzymes are implicated in both solid and hematological tumors; he would not say which indications Accent plans to target first or when it expects to select its first clinical candidate.

Only one other company — Storm Therapeutics Ltd. — has been formed to target RNA-modifying proteins. Storm spun out of the University of Cambridge in 2016. Like Accent, it has a pipeline of discovery stage small molecules against undisclosed targets. Copeland said Storm has not disclosed enough detail about its approach to compare it with Accent's.

At least three companies — Expansion Therapeutics Inc., Arrakis Therapeutics Inc. and Ribometrix Inc. — emerged over the last three years to develop small molecules that target RNA transcripts directly to treat cancer other diseases, rather than indirectly through RNA-modifying enzymes. While those companies also aim to expand target space, according to Copeland, the advantage of modulating RNA-modifying enzymes is that the proteins regulate multiple transcripts, and should produce broader effects on gene expression patterns.

Copeland said it's too early to discuss Accent's plans for partnering, although he sees potential for the biotech to build out an internal pipeline while executing a collaboration with a strategic partner.

The company has not yet filed any patent applications for its technology. bc

ACCENT THERAPEUTICS INC.
Lexington, Mass.

Technology: Small molecule inhibitors of RNA-modifying proteins to treat cancer

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2017 by Robert Copeland, Howard Chang and Chuan He

University collaborators: Stanford University, University of Chicago

Corporate partners: None

Number of employees: 1

Funds raised: $40 million

Investors: The Column Group, Atlas Venture and EcoR1 Capital

CEO: None

Patents: None issued

COMPANIES AND INSTITUTIONS MENTIONED

Accent Therapeutics Inc., Lexington, Mass
Arrakis Therapeutics Inc., Waltham, Mass.
Expansion Therapeutics Inc., San Diego, Calif.
Ribometrix Inc., Chapel Hill, N.C.
Stanford University, Stanford, Calif.
Storm Therapeutics Ltd., Cambridge, U.K.
University of Chicago, Chicago, Ill.

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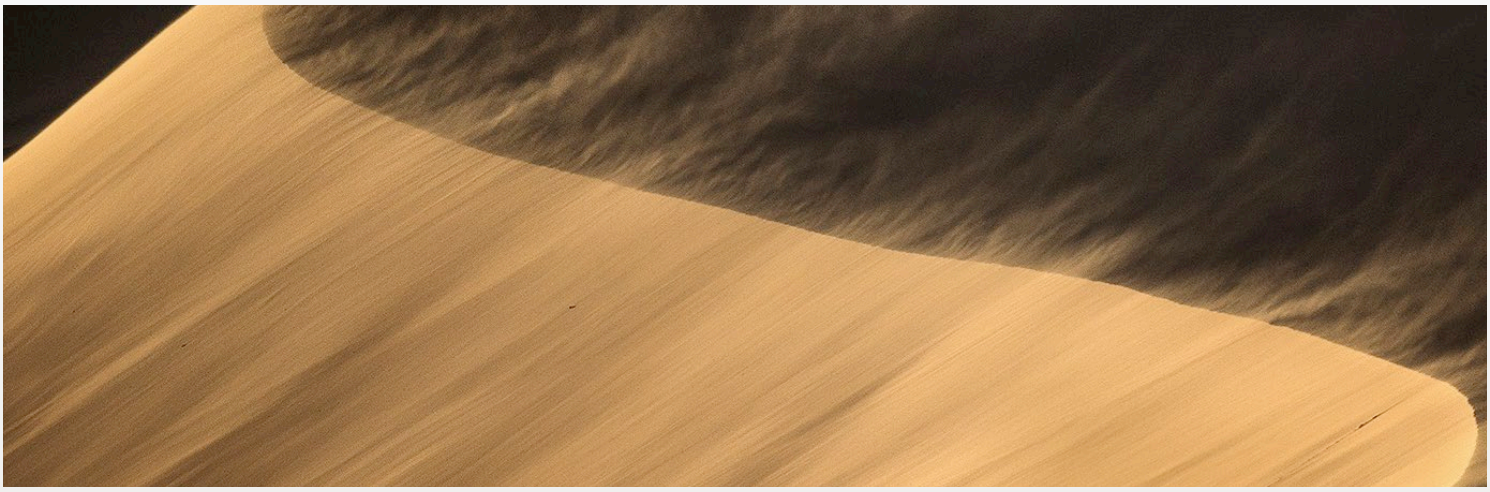

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POLITICS, POLICY & LAW

SHIFTING PARTS

BY STEVE USDIN, WASHINGTON EDITOR

HHS Secretary Alex Azar is convinced that the way Medicare Part B spends money for drugs makes no sense, costs the taxpayers too much and isn't good for patients. He says he's open to suggestions from drug companies about ways to change it, and if they don't come up with acceptable ideas for increasing competition, he'll impose changes the industry won't like.

Azar's preference for replacing the system of purchasing drugs under Part B, which covers medicines administered under a physician's supervision, is to shift those drugs into Part D, which was created to cover drugs purchased from pharmacies.

From the perspective of CMS, the biggest difference between the systems is that Part B pays the average sales price (ASP) plus a 6% administration fee, while Part D uses private plans to negotiate prices and impose utilization management controls.

For many patients, however, the difference is that supplemental insurance eliminates or sharply reduces out-of-pocket costs in Part B, while Part D imposes costs that can put drugs out of reach.

CMS's challenge, if it shifts drugs from Part B to D, is to secure savings for the taxpayer without imposing crushing costs on patients.

In 2015, the most recent year for which the Government Accountability Office provided a total, Part B spent $26 billion on drugs.

Azar has made it clear that he is open to ways of changing Part B drug purchasing other than shifting to Part D, including reviving a failed experiment, the Competitive Acquisition Program (CAP), that ran from 2005 to 2007. Under CAP, private vendors served as middlemen between drug manufacturers and medical practices.

Azar hasn't announced timelines for achieving the changes he envisions. It would be impossible to implement large-scale restructuring of Medicare drug payment policies in 2019 and will be challenging to get them into place in 2020.

This gives pharma, providers and patients time to engage with HHS to reshape the Medicare drug purchasing environment — or to mobilize opposition (see "Azar's Razor").

Industry hasn't decided whether it will work with Azar or try to obstruct his efforts in the hope of running out the clock on the Trump administration. PhRMA's board of directors will meet June 1 to discuss the trade association's response to the administration's drug pricing blueprint, including its Part B provisions.

Because Azar can accomplish most of his goals through the power of his pen, corporate America's preferred tools for influencing public policy, armies of lobbyists and buckets of campaign contributions, will be blunted. Industry's attempts to sway the executive branch are more likely to focus on the deployment of surrogates, including patient and medical groups.

DUMPING DRUGS FROM PART B

Under Part B, the government is "paying sticker plus a markup," Azar told reporters at a briefing on May 14.

Relying on physicians and hospitals to purchase drugs and then reimbursing them ASP plus 6% ensures that government overpays, and creates financial incentives for physicians to prefer the most expensive therapeutic alternative, according to Azar.

"I fundamentally believe we should move to a system where doctors have no financial incentive in terms of the drugs they are prescribing," he said.

Although HHS isn't even close to having firm plans for what it will do to Part B, Azar is adamant that there will be changes, and that it would be in the best interests of biopharma companies to help determine how to design them.

"We are going to bring negotiation to Part B drugs," he said at a May 16 meeting sponsored by the American Enterprise Institute and the University of Southern California-Brookings Schaeffer Initiative for Health Policy.

"It is going to happen, so it would be most productive if the pharmaceutical industry came to us with plans for these changes," Azar said. "If pharma doesn't come to us with a plan about which drugs it makes sense to move from Part B to D, we'll decide that for them."

Shifting drugs from Part B to D makes sense "so they are being paid under the same regime, fighting against each other, being put on formularies [and] controlled with appropriate utilization management," Azar said.

While the ultimate goal is to merge all of Part B drug purchasing into Part D, HHS is considering several options for starting the process.

The shift could initially be limited to therapeutic classes where drugs are purchased both by Part B and by Part D, he said. Some conditions can be treated by biologics that are infused and by small molecule drugs. In addition, many drugs can be purchased and administered either under a physician's direction or from a pharmacy, so they are purchased by both Part B and Part D.

Alternatively, HHS could use the results of a study it is conducting of disparities between U.S. pricing and prices in other The Organisation for Economic Co-operation and Development (OECD) countries to target Part B drugs that are much more expensive in the U.S. than in other industrialized countries, Azar said.

WOULD SHIFTING FROM B TO D SAVE?

HHS has not modeled the economic effects of shifting drugs from Part B to D, but Azar has no doubt it would produce substantial savings. "I believe it will save patients out of pocket; I know it will save the taxpayers," he told reporters.

The savings, he said, will result from applying the tools Part D plans use to negotiate prices. He suggested the savings could be large enough that some Part D plans could provide the drugs on terms that are at least as attractive for patients as the terms under Part B.

Experience with drugs purchased under both Part B and Part D provides insights into the pricing side of the equation.

According to the CMS Medicare Drug Spending Dashboard, Part B paid $9,814 per patient for Lucentis ranibizumab from the Genentech Inc. unit of Roche in 2016, spending $1.04 billion to treat 106,408 patients. Medicare paid an average of $8,380 for the 334 patients who received Lucentis under Part D in 2016.

Remicade infliximab from Johnson & Johnson cost Part B an average of $22,925 per patient for 58,397 patients in 2016. Medicare Part D paid an average of $28,282 per patient for 2,407 patients.

The Part B figures for both drugs reflect all of Medicare's costs. The Part D figures, however, are almost certainly overestimates because they do not reflect manufacturer rebates or price concessions.

Given the large numbers of patients who use Lucentis and Remicade, and the availability of therapeutic alternatives, Part D plans would have a great deal of leverage to negotiate lower prices.

In addition, there is no way to know whether utilization management tools, such as requiring copays or prior authorization, would suppress demand in Part D.

> "WE SHOULD MOVE TO A SYSTEM WHERE DOCTORS HAVE NO FINANCIAL INCENTIVE IN TERMS OF THE DRUGS THEY ARE PRESCRIBING."
>
> ALEX AZAR, HHS

OUT-OF-POCKET COSTS

Ensuring that patients aren't hurt by shifting from B to D will be crucial, and a challenge, James Scott, president & CEO of healthcare consulting firm Applied Policy, told BioCentury.

Scott said Azar's objections to the Part B drug scheme make a great deal of sense from the taxpayer perspective. "The real problem is that Medicare Part B is an unmanaged benefit, with very few coverage policies, nothing limiting prescribing to on-label uses or those in guidelines, and the 6% administration fee rewards physicians for choosing the most expensive among alternatives," he noted.

The patient perspective, however, could be quite different.

While patients who obtain drugs under Part B are responsible for a 20% coinsurance payment, the "vast majority of Medicare beneficiaries have supplemental insurance, so even though the drugs are very expensive, a lot of times the patient's obligation is zero," Scott noted.

In 2013, 81% of Medicare beneficiaries had supplemental coverage, according to the Kaiser Family Foundation.

For drugs that cost more than $670 per month, Medicare Part D plans can charge up to a 33% coinsurance fee. Supplemental insurance cannot be used to offset out-of-pocket costs under Medicare Part D.

As a result, even Part B beneficiaries who do not have supplemental coverage could pay more out-of-pocket if a drug were shifted from Part B to D.

"It will be important for the administration to consider these factors as it considers whether some Part B drugs should be reimbursed under Medicare Part D to make sure the move isn't just good for the government's bottom line, but is also good for consumers," Scott said.

An analysis conducted by Avalere Health LLC illustrates the complexity of determining the effects of shifting drugs from B to D.

The analysis included a basket of drugs that were approved for new indications including lung, intestinal, breast, ovarian and pancreatic cancers and melanoma, myeloma and lymphoma. The Part D drugs were oral therapies, and the Part B drugs were administered by physicians. All the drugs had been approved for these indications for one year or less.

In 2015 and 2016 about 14,000 Part D enrollees who were not eligible for low-income subsidies paid an average of $4,400 in out-of-pocket costs for new cancer therapies, and their average gross drug costs were $70,000. Gross drug costs include total spending for the prescription claim by the patient, plan and government, but exclude manufacturer rebates paid to plans.

During the same period, about 2,000 Part B enrollees who did not have supplemental insurance paid an average of $9,700 for new cancer therapies, and their average ASP+ drug costs were $48,000.

This analysis demonstrates that a shift from Part B to D would result in higher out-pocket costs for the minority of Part B enrollees who do not have supplemental coverage. While the analysis was conducted on selected cancer drugs, Avalere told BioCentury results would be similar for other high-cost drugs.

Complicating the analysis further, more people are enrolled in Part B than in Part D. Holly Campbell, deputy VP for public affairs at PhRMA, ballparked the figure at "hundreds of thousands" of beneficiaries. Some of those patients who would have had access to drugs under Part B may be unable to afford them if they are shifted to Part D, Campbell said.

"Proposals to merge Part B coverage of medicines into Part D could increase patient costs and reduce access," she told BioCentury.

Sorting through the claims and counter-claims about the effects on patients will be a complex, time-consuming process.

If the policies are implemented through a proposed rule, CMS would be legally required to produce an actuarial analysis. There are bureaucratic alternatives that would not require economic reporting.

Azar has said he will develop drug policy in a transparent manner. This suggests that CMS will release analyses of the costs and coverage implications of its proposals before they are put into effect.

REVIVING CAP

In addition to shifting drugs from Part B to D, the Trump administration is considering reviving CAP.

CAP was authorized by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. The idea was to allow physicians to opt out of the Part B buy-and-bill process.

CMS solicited bids in 2005 from vendors who would purchase drugs from manufacturers and provide them to physicians. CAP went into effect in 2005 and was suspended in 2008 because it didn't attract enough of vendors.

The economic environment has changed a great deal since 2008, with Part B supplying multiple competing high-priced drugs, so there could be more interest on the part of potential middlemen, Azar told reporters.

A revival of CAP, "or a model building on CAP authority, may provide opportunities for Federal savings to the extent that aggregate bid prices are less than 106 percent of ASP," according to the Trump administration's prescription drug pricing plan. It would also provide "opportunities for physicians who do not wish to bear the financial burdens and risk associated with being in the business of drug acquisition."

CAP, or something like it, could leverage restrictive formularies to negotiate prices. While doing so would reduce prices, it could also raise concerns among patients and physicians about restrictions on access to therapies.

POWER OF THE PEN

Azar told reporters he believes CMS has authority to implement changes to Medicare drug payment under the Affordable Care Act (ACA), which

AZAR'S RAZOR

In pushing for restructuring the ways Medicare purchases drugs, HHS Secretary Alex Azar is applying insights into drug company tactics and industry pressure points gleaned over a decade as a senior executive at Eli Lilly and Co., including five years as president of Lilly USA.

Azar also served on BIO's board of directors.

He seems to have coined a new version of Occam's razor. Azar's razor could be defined as "the louder pharma complains about a drug pricing policy, the more likely it is to be good for patients and the public."

He nodded to this principle in remarks to a meeting sponsored by the American Enterprise Institute and the University of Southern California-Brookings Schaeffer Initiative for Health Policy on May 16, saying: "Bringing negotiation to Part B drugs is such a potent way to bring down prices that pharma is already protesting the idea — this is really on their list of worst nightmares."

Azar also noted a statement from PhRMA expressing concern that the administration's plans for Part B drugs could pose threats to patient affordability and access. BIO issued a similar statement.

"I beg to differ," Azar said. "The single greatest threat to patient affordability and access to prescription drugs in America is the high list prices, set by drug companies and encouraged by today's system. Negotiating these prices down isn't a threat to patients — it's the solution they need."

He also recalled that drug companies "have insisted that we can have new cures or affordable prices but not both," a notion that he ridiculed.

"I've been a drug company executive, so I know the talking points pretty well: the idea that if one penny disappears from pharma profit margins, American innovation will grind to a halt. The President and I are tired of these talking points," he said.

— Steve Usdin

created the Center for Medicare & Medicaid Innovation (CMMI) and gave it power to test innovative payment and service delivery models.

"We believe it is within our authority to use demonstration authorities, as well as the innovation authority within CMMI, to experiment with changing Part B into Part D drugs, and we will not hesitate to do so," Azar told reporters.

CMS tried to use CMMI to restructure Part B under the Obama administration, proposing in March 2016 to reduce the ASP fee to 2.5% for physician practices in about 75% of the country while retaining 6% for the remainder. This was intended to be the first stage of a plan that would include experimenting with value-based payment models.

Biopharma companies, oncologists and rheumatologists, and patient groups attacked the plan.

A letter from 179 Republican members of Congress protesting the CMMI Part B demonstration said CMS "exceeded its authority, failed to engage stakeholders, and has upset the balance of power between the legislative and executive branches."

The criticism forced CMS to withdraw the plan.

Azar told reporters that his use of CMMI to alter Part B drug payments wouldn't meet the same fate. He called the Obama administration's plan a "simple price control" that would have been achieved by "cramming down the 106%" of ASP formula.

Moving drugs to Part D "retains beneficiary choice" because there will be a multitude of Part D plans with different benefit designs, Azar said.

He also noted that ASP-based reimbursement hurts physicians, especially those with low-volume practices, who are unable to purchase drugs at or below the average sales price.

A key to building political support for the plan will be limiting the number of interest groups that oppose it.

If HHS finds a way to ensure that patients' costs do not increase, and to compensate physicians and medical practices for administering drugs, it would neutralize two sets of potential opponents. bc

COMPANIES AND INSTITUTIONS MENTIONED

American Enterprise Institute, Washington, D.C.
Biotechnology Industry Organization, Washington, D.C.
Brookings Institution, Washington, D.C.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Genentech Inc., South San Francisco, Calif.
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Kaiser Family Foundation, San Francisco, Calif.
Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
University of Southern California, Los Angeles, Calif.
U.S. Department of Health and Human Services, Washington, D.C.

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EBB & FLOW

SINGLE CELSIUS

BY CHRIS LIEU, STAFF WRITER

After identifying its first targets, Third Rock Ventures newco Celsius Therapeutics emerged from stealth with a $65 million series A round to apply single-cell genomics techniques to drug development for autoimmune diseases and cancer.

GV, Heritage Provider Network, Casdin Capital, Alexandria Venture Investments and undisclosed other investors also participated in the round.

Third Rock's Christoph Lengauer, who serves as the newco's president, told BioCentury Celsius is the first therapeutics company to leverage single-cell genomics rather than the traditional genomic sequencing approach, which he said is limited by low resolution given that traditional sequencing data come from an average of several cell types, rather than individual cells.

Single-cell genomics, in contrast, allows researchers to determine specific cell types that contribute to or drive disease, according to Lengauer. "The understanding of a cell, its neighborhood and cell-to-cell interactions — that's the value proposition of this technology."

Celsius' platform and programs originated in the labs of Aviv Regev and Vijay Kuchroo. Regev is a professor of biology at Massachusetts Institute of Technology and member at the Broad Institute of MIT and Harvard, and Kuchroo is a professor of neurology at Harvard Medical School and associate member at the Broad Institute.

Celsius has a non-exclusive license to single-cell sequencing technologies and an exclusive license to undisclosed early stage programs from the Broad Institute.

"Aviv and her colleagues defined cell types that we didn't know exist, both for the microenvironment in the immune cell space and in complex diseases," said Lengauer.

He said that during its two years in stealth mode, Celsius had been working on increasing single-cell resolution, developing machine learning algorithms to identify specific cells and genetic mutations within those cells that drive disease states, and identifying undisclosed targets.

Celsius will use the data to develop small molecules, biologics and recombinant proteins for genetically defined patient populations, and plans to use the A round to obtain preclinical proof of concept and identify lead programs.

Lengauer said GV, which is the venture arm of Alphabet Inc. (NASDAQ:GOOG), "was a natural fit" for the syndicate given the large and complex data sets the company is generating.

"Single cell biology is likely to be the centerpiece of the next phase of genomic research, allowing us to go from genetic variants that are implicated in disease to the active cell types and molecular mechanisms," GV's Anthony Philippakis told BioCentury.

Earlier this month, Third Rock and GV co-invested in insitro Inc., another machine learning-based drug discovery play.

Third Rock has launched three other companies this year with average series A funding of $58.2 million. It was the sole investor in each of those rounds.

> "THE UNDERSTANDING OF A CELL, ITS NEIGHBORHOOD AND CELL-TO-CELL INTERACTIONS — THAT'S THE VALUE PROPOSITION."
>
> CHRISTOPH LENGAUER, THIRD ROCK

NSUN'S CHINA AMBITIONS

BY JENNIE WALTERS, STAFF WRITER

The China-heavy syndicate behind Ansun BioPharma Inc.'s $85 million series A round reflects the San Diego-based antiviral company's long-term plans to penetrate the China market.

Sinopharm Healthcare Fund and Lilly Asia Ventures led the round, with participation from fellow new Chinese investors Lyfe Capital, Yuanming Capital, Matrix Partners China, 3e Bioventures Capital, Oceanpine Capital, VI Ventures and Joincap Investment. Ansun interim CEO Nancy Chang said undisclosed U.S.-based investors also participated.

"There's a significant interest in antivirals in China, especially those directed at flu, because pandemic strains of flu tend to come out of China or other parts of Asia," said Mike Havluciyan, Ansun's general counsel and SVP of operations.

Ansun's lead candidate, DAS181 (Paradase, Fludase), is slated to enter Phase III testing early next year to treat parainfluenza virus in hospitalized, immunocompromised patients. DAS181, a recombinant fusion protein consisting of a sialidase functional domain fused with an amphiregulin glycosaminoglycan-binding sequence, has Fast Track and breakthrough therapy designations in the U.S. for parainfluenza virus.

Lyfe's James Zhao said the VC had been following Ansun's progress for nearly a year, noting that there are "huge unmet needs" for flu treatments, and China and the U.S. comprise the two largest markets. "China demonstrates a strong market potential for Ansun in the future," Zhao added.

Lyfe invests in U.S. and Chinese companies alike to connect them with the firm's cross-border networks. Beyond capital, Zhao said Lyfe could provide Ansun with local resources and support for clinical trials and marketing in China (see BioCentury, June 9, 2017).

Havluciyan said China development would "ideally" parallel U.S. development for quicker patient access, but said the company is in the early stages of developing its China strategy.

Ansun launched in 2003 and raised about $150 million prior to the series A round, including $90 million in government funding and $60 million from private investors and family offices. Chang said the series A investors were Ansun's first institutional investors.

Ansun was one of at least three U.S. biotechs to raise venture rounds led by Chinese investors this week. On May 16, stapled peptide company Fog Pharmaceuticals Inc. closed a $66 million series B round led by 6 Dimensions Capital and antibody play HiFiBiO Therapeutics raised $37.5 million in a series B round led by Sequoia China and Lyfe.

"CHINA DEMONSTRATES A STRONG MARKET POTENTIAL FOR ANSUN IN THE FUTURE."

JAMES ZHAO, LYFE CAPITAL

CELLCENTRIC'S MAGIC TRIO

BY VIRGINIA LI, ASSISTANT EDITOR

Five years after pivoting from target discovery to drug development, epigenetics play CellCentric Ltd. is taking its sole asset CCS1477 into the clinic next month with $26 million from Morningside Venture Investments. The company believes the undisclosed venture round will be enough to get the prostate cancer compound through clinical proof-of-concept studies.

Morningside first invested in CellCentric in 2007.

Morningside's Jason Dinges said that at the time, CellCentric "was focused broadly on epigenetics, but was more using its biology expertise to identify interesting targets, then collaborate with partners to develop those targets to then be out-licensed."

Chairman and CEO Will West said CellCentric shifted to an asset-centric model in 2013.

"A lot of pharma companies were starting to build their own in-house capacity in epigenetics, so they were less reliant on early stage programs from external sources. We decided that if we were going to play in this space, we had to pick a program and get behind it," said West. "By that stage, we had looked at around 50 different oncology targets and worked on seven."

Dinges said, "What drew Morningside to the company was the deep biology expertise the company had in epigenetics. We respect their expertise in this field and have continued to support them as they've moved CCS1477 towards the clinic."

West said the dual inhibitor of E1A binding protein p300 (EP300; p300) and CREB binding protein (CREBBP; CBP) had "the magic trio of working out the biology, the chemistry and having a decent commercial opportunity."

EP300 and CREBBP are highly homologous transcriptional co-activators of the androgen receptor signaling pathway — a well-established prostate cancer target.

EP300 and CREBBP have also emerged as epigenetic cancer targets of interest to pharmas in the past year. AbbVie Inc. (NYSE:ABBV) and the Genentech Inc. unit of Roche (SIX:ROG;

"WE HAD TO PICK A PROGRAM AND GET BEHIND IT."

WILL WEST, CELLCENTRIC

OTCQX:RHHBY) have published preclinical data on the role of these targets in prostate and hematological cancers. Neither company has disclosed development plans for dual EP300 and CREBBP inhibitors (see BioCentury Innovations, Oct. 26, 2017).

Last year, CellCentric reported data showing CCS1477 led to complete tumor growth inhibition in a xenograft mouse model of castration-resistant prostate cancer (CRPC).

West said rather than grow the pipeline, the aim is to sell the company after a to-be-determined inflection point for CCS1477.

He said the company also plans to bring CCS1477 to the clinic by year end for multiple myeloma and acute myelogenous leukemia (AML), and by 3Q19 for lung and bladder cancer.

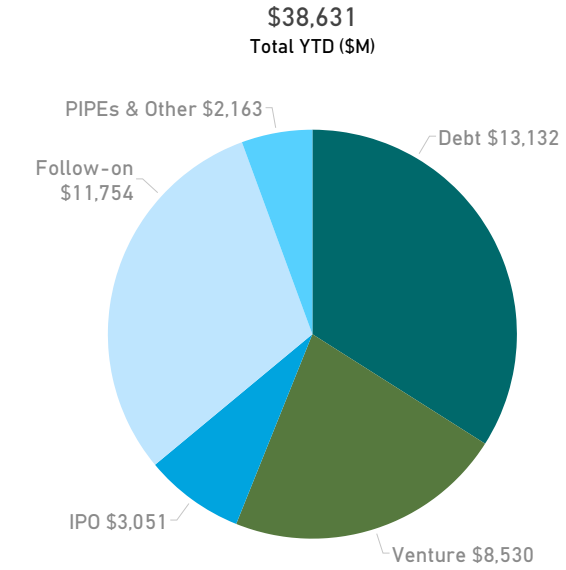
Prior to the latest round, CellCentric had raised a total of $22 million in venture funding, plus $6 million through a combination of government funding and target discovery deals. bc

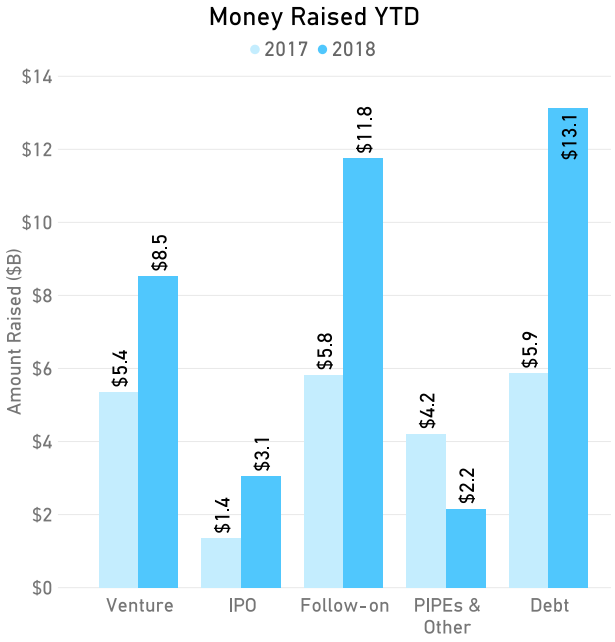
CLARIFICATION

Taiwanese securities regulations prohibited insiders from participating in the May 4 NASDAQ offering by Aslan Pharmaceuticals Ltd. (TPEx:6497; NASDAQ:ASLN). The regulations prohibit shareholders over a certain threshold and those sitting on a company's board from participating in public stock offerings by companies listed on Taiwan's stock exchange. Aslan said other existing investors, including Temasek and Morningside, bought over 60% of the NASDAQ deal.

MONEY RAISED IN 2018

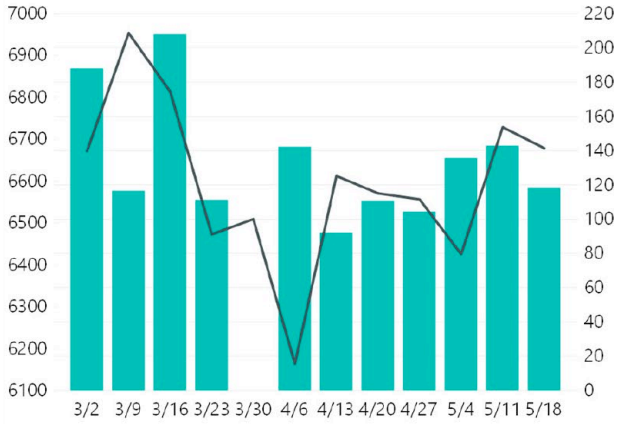
Last week, the biotech industry raised $2.3 billion, bringing to $38.6 billion the total raised year-to-date. Totals include overallotments and warrants, and are rounded to the nearest millions.





BIOCENTURY 100 PRICE & VOLUME

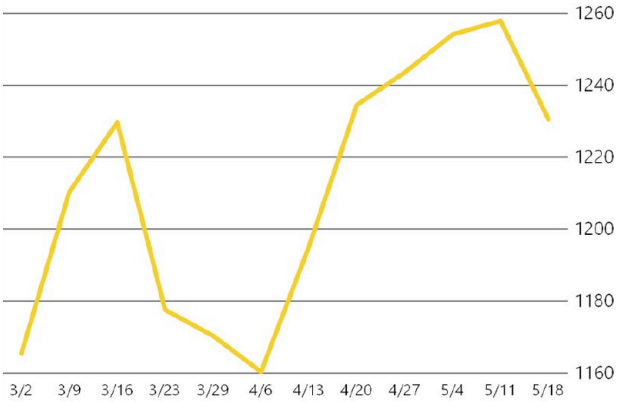
Cumulative weekly price (line, left scale) and volume in millions (bars, right scale) of 100 biosciences stocks over the past 12 weeks; prices indexed to 1,000 on May 10, 1996



BioCentury tracks 852 issues that report prices and volume daily. The BioCentury 100 is a subset used to monitor price and volume trends.

BIOCENTURY LONDON INDEX

Weekly change in the combined market capitalization of 14 bioscience stocks listed on the LSE or AIM over the past 12 weeks; indexed to 1,000 on May 10, 1996



BIOCENTURY 100 INDICATORS

Week ended 5/18/18

Prices	Volume
6678.21	618.3M shrs
-0.75%	-15.47%

PRICE GAINS

Stocks with greatest % price increase in the week ended 5/18; price above $2; 5,000 minimum share volume

Company	Ticker	Close	Chg	%Chg	Vol (00)
Emisphere	EMIS	$2.21	0.86	64%	42257
MEI Pharma	MEIP	$3.46	1.23	55%	90869
Eiger	EIGR	$13.9	3.90	39%	33737
Galectin Therapeutics	GALT	$4.56	1.20	36%	79287
BioDelivery	BDSI	$2.3	0.60	35%	134098
CytoSorbents	CTSO	$10.55	2.50	31%	38227
Quotient	QTNT	$6.05	1.35	29%	65298
TapImmune	TPIV	$3.69	0.81	28%	9602
Alpine Immune Sciences	ALPN	$9.95	2.07	26%	1279
Sophiris	SPHS	$3.61	0.72	25%	66681

PRICE DECLINES

Stocks with greatest % price decline in the week ended 5/18; price above $2; 5,000 minimum share volume

Company	Ticker	Close	Chg	%Chg	Vol (00)
Jounce Therapeutics	JNCE	$11.37	-5.41	-32%	107613
Noxxon	ALNOX	€3.87	-1.37	-26%	779
resTORbio	TORC	$9.24	-2.72	-23%	9066
Celyad	CYAD	$26.9	-6.65	-20%	2965
Sensorion	ALSEN	€2.95	-0.67	-19%	17362
Molecular Templates	MTEM	$7.26	-1.62	-18%	3623
Syndax	SNDX	$8.8	-1.89	-18%	90222
Synlogic	SYBX	$9.8	-1.96	-17%	5816
Evofem	EVFM	$5.4	-1.00	-16%	1288
Opiant	OPNT	$16.16	-2.77	-15%	1855

VOLUME GAINS

Stocks with greatest % gain in volume above 5,000 shares

Company	Ticker	Vol (00)	%Chg	Close	Chg
GlycoMimetics	GLYC	754000	2706%	$18.41	-0.08
BioBlast Pharma	ORPN	61685	2267%	$2.26	-0.24
Celyad	CYAD	13111	1081%	€27.76	-5.82
ObsEva	OBSV	13124	1059%	$13.3	0.70
Zymeworks	ZYME	10255	727%	C$17.17	1.30
Sensorion	ALSEN	17362	677%	€2.95	-0.67
Summit Therapeutics	SMMT	4562	607%	L2.7	0.09
GTx	GTXI	25611	545%	$18.6	1.27
AB Science	AB	75365	469%	€5.62	-0.22
Avenue Therapeutics	ATXI	1265	448%	$4.25	0.37

BC100 ADVANCE-DECLINE TRENDS.

Week Ended	BC100 Index	Gainers	Gaining Volume	Decliners	Declining Volume
5/18/18	6678.21	64	404,657,479	35	212,683,169
5/11/18	6728.49	72	540,182,421	28	191,290,259
5/4/18	6425.38	48	227,617,890	51	408,317,595
4/27/18	6556.22	51	300,567,973	47	276,328,020
4/20/18	6570.59	45	242,800,364	53	275,928,385

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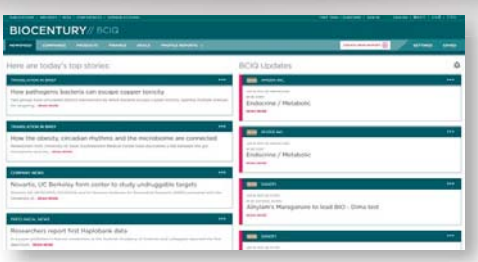

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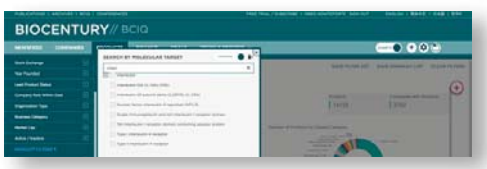

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