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BY JOHN HODGSON AND MIKE WARD

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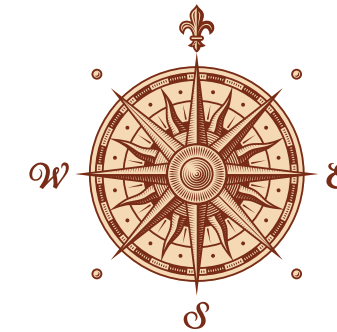
European Life Sciences Start-Ups Maintain Early Investor Allure

BY JOHN HODGSON AND MIKE WARD

Data compiled by Informa Pharma Intelligence confirms that European life sciences companies witnessed a year-on-year increase in venture cash put to work in 2017. Indeed, European life sciences pocketed more than twice what they raised just five years ago even though the number of companies raising that money has barely moved over the same time period.

Investors continue to raise additional venture money that is being earmarked for European investments as they seek to tap assets that are less expensive than those being developed by US companies. While much of the venture money raised by European life sciences companies comes from more local sources, the amount coming from non-European sources continues to rise.

So what? Quality European companies with compelling assets, technologies and data will find it easier to attract increasing amounts of venture financing as investors back larger rounds. But accessing non-specialist capital from the public markets is likely to remain a major challenge forcing businesses to focus their attention on the deeper pools of capital available to companies listing on US exchanges.



Venture capital investment in life sciences companies continues to rise. In 2017, biopharma and medtech start-ups raised \$19.7 billion worldwide. European businesses retained a robust share of that global take and investors expect that trend to continue.

It has never been a better time for life sciences start-ups to raise money from venture sources. In 2017, according to data compiled by Informa Pharma Intelligence, venture capitalists invested a total of \$19.7 billion in the sector across the globe – some \$15.1 billion allocated to 512 biopharma-focused opportunities while \$4.6 billion was invested in 107 medtech businesses. Europe's share of the global take was nearly \$4 billion, more than double what it was in 2013.

With new funds being raised and non-European investors looking for bargains, the prospects for European biopharma, medtech and digital health companies going forward looks fairly robust. (See Exhibit 1.) However, there are some clouds on the horizon. While the opportunities to raise seed and Series A money in Europe remain buoyant, returning to the capital markets – whether private or public – for the larger boluses of cash required to accelerate growth into sustainable businesses will continue to be a challenge. Moreover, European medical device companies might find raising venture capital more difficult as the regulatory environment becomes more complex.

European biotech entrepreneurs need to be aware that the venture capital industry has other opportunities to get healthy returns. Indeed, European VCs

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have put similar amounts of money into finance ventures or Internet companies or into consumer enterprise or business services. Looking across all venture investments, health-related VC is around 20% of the \$22 billion total in Europe, estimated by FinSMEs, a pan-sectoral investment website. Biotech accounts for around 14% of the total and medtech for about another 3%.

Life sciences companies come out well as recipients of big ticket venture backing, attracting seven of the declared 19 A, B or C rounds in Europe above \$50 million in 2017. (See Exhibit 2.) However, as if to prove that author Douglas Adams was right all along, the leading B round in Europe in 2017 went to **Improbable**, a British software company developing huge-scale virtual world simulations. It attracted \$502 million, just short of the \$511 million that the seven big ticket life sciences companies got between them.

Investment in Improbable was led by Softbank Vision, the Japanese-Saudi unicorn backer that also was involved in the CHF1.1 billion investments into pharma developer **Roivant Sciences GMBH** in Switzerland and the \$360 million late venture round into US liquid biopsy specialist, **Guardant Health Inc.**

European Venture Capital Patterns And Exits

Venture capitalists are opportunists, albeit informed ones. Where their money goes depends not only on the qualities of

Exhibit 1
New Money: Funds Raised Since Start Of 2017 That Can Be Deployed In Europe

INVESTOR	FUND NAME	MOST RECENT CLOSE	VALUE \$M	GEOGRAPHIES	FOCUS	KEY INVESTMENTS MADE TO DATE
Edmond de Rothschild Investment Partners	BioDiscovery 5	01/18	428	70% EU, 30% RoW	2/3 Therapeutics, 1/3 Medtech; mainly private	Erytech Pharma SA, Complexa Inc, LogicBio Therapeutics Inc
Athyrium Capital Management & Neuberger Berman	Athyrium Opportunities Fund III	12/17	1,200	80% US, 20% RoW	50% revenue generating biopharma; 50:50 public:private	OB Hospitalist Group, DuPage Medical Group
BioGeneration Ventures	BGV III	10/17	95	Seed funding of Benelux & German life science firms	Early stage therapeutic, medtech & diagnostics	NorthSea Therapeutics BV, Mellon Medical BV, VarmX BV, Escalier Biosciences BV
BioMedPartners	BioMedInvest III	08/17	105	Switzerland, Germany, Austria, France, Italy & Benelux	Private early- to mid-stage human life Science firms in therapeutics, medical devices & diagnostics	Allegra Therapeutics GmbH, AMAL Therapeutics SA, Cardior Pharmaceuticals GmbH
Bay City Capital & GF Xinde Investment Management Co. Ltd	Bay City Capital GF Xinde International Life Sciences Fund	07/17	200	Global with focus on US, Canada, Western Europe & China	All stages of development for innovative biopharma approaches	Twist Bioscience Inc, KBP Biosciences, Occulis
Atlas Venture	Atlas Venture XI	06/17	350	Global	Early stage	Three undisclosed investments in stealth mode are in incubation
Medicixi	Medicixi Growth 1 (MG1) Fund	06/17	300	80% European, 20% US	Growth companies with ideas beyond proof of concept & robust clinical data	ObsEva SA
Vesalius Biocapital Partners	Vesalius Biocapital III	05/17	73	European	80% later-stage life science firms in drug development (50%), medtech, diagnostics & eHealth/mhealth	
Ping An Insurance Company of China Ltd	Ping An Global Voyager Fund	04/17	1,000	Global specifically in the US, the UK & Israel excluding China	Invests in early-stage fintech & digital health start-ups	TytoCare Ltd, StartUp Health
Mitsubishi UFJ Financial Group Inc	Mitsubishi UFJ Life Science I LP	03/17	89		Seed to late stage investments in therapeutics, regenerative medicine, medical devices & diagnostics	None announced as yet
Seroba Life Sciences	Seroba Life Sciences Fund III	02/17	108	Mainly Irish (50%), UK & Europe with US an option	New companies developing drugs or medical devices	Endotronix Ireland, Prexton Therapeutics SA
Advent France Biotechnology	Advent France Biotechnology Seed-Fund I	04/17	75	Early French		None announced
Arix Bioscience plc	Raises money from public market	02/17	117	Late-stage US and European		Autolus, Verona Pharma, Artios Pharma
High-Tech Gruenderfonds	High-Tech Gruenderfonds III	06/17	280	Mainly early German	Wide range of tech and biology	Zimmer Biotech, Cysal, Venneos GmbH, Sirion Biotech

SOURCE: In Vivo research

Exhibit 2
European A-C Rounds Worth More Than \$50M In 2017

ROUND SIZE \$M	ROUND	COMPANY	BUSINESS	COUNTRY
502	B	Improbable	Simulations	UK
165	B	Tricentis	Software testing	Austria
110	B	Orchard Therapeutics	Gene therapy	UK
90	B	Lilium	Electric jet planes	Germany
85	C	Cell Medica	Immunotherapy	UK
80	C	Autolus	T cell therapy	UK
70	C	ManoMano	DIY marketplace	France
66	B	Revolut	Banking	UK
65	B	Iterum Therapeutics	Pharmaceuticals	Ireland
65	B	Innoviz Technologies	Automotive sensor	Israel
60	B	Bicycle Therapeutics	Peptide platform	UK
60	A	MessageBird	SMS platform	Netherlands
59.6	C	Hookipa Biotech	Biopharmaceuticals	Austria
56	C	AppsFlyer	Data collection by apps	Israel
51.75	C	Xeltis	Heart valve restoration	Netherlands/Switzerland
51.75	B	Simba	Mattress maker	UK
50	B	Receipt Bank	Bookkeeping	UK
50	B	Oryx Vision	Autonomous vehicle sensing	Israel
50	C	Graphcore	Chip design	UK

SOURCE: FinSMEs

the supplicant companies but also on the routes for getting exits. In the US, public market exits mean Nasdaq but in Europe, options differ.

France, the Netherlands and Belgium have a network of related public stock exchanges designed for small or medium-sized companies – Euronext and Alternext – while the companies in the Nordic region have access to the Nasdaq First North. In theory, all appropriately certified companies have access to these markets, but practical barriers to a single financial market persist.

Nevertheless, the existence of these newish and more adventurous public markets seems to have influenced patterns of venture investment, as Exhibit 3 illustrates.

In France, the Nordic countries and

Benelux, venture funding in life sciences seems almost to be completely focussed on small pre-A and A rounds, with subsequent venture rounds both small and sporadic. This may be because there is an option for companies to list early on Euronext, Alternext or Nasdaq First North.

In contrast, elsewhere in Europe, venture capital in 2017 not only persisted beyond A rounds to B and C and beyond, but the later rounds were often substantial. Rounds in excess of \$50 million were not uncommon, particularly in the UK where \$50 million-plus rounds appeared in B series financings, too, for two biotech companies, **Orchard Therapeutics** and **Bicycle Therapeutics Ltd.** and for digital health play, **Babylon Health.** (See Exhibit 4.)

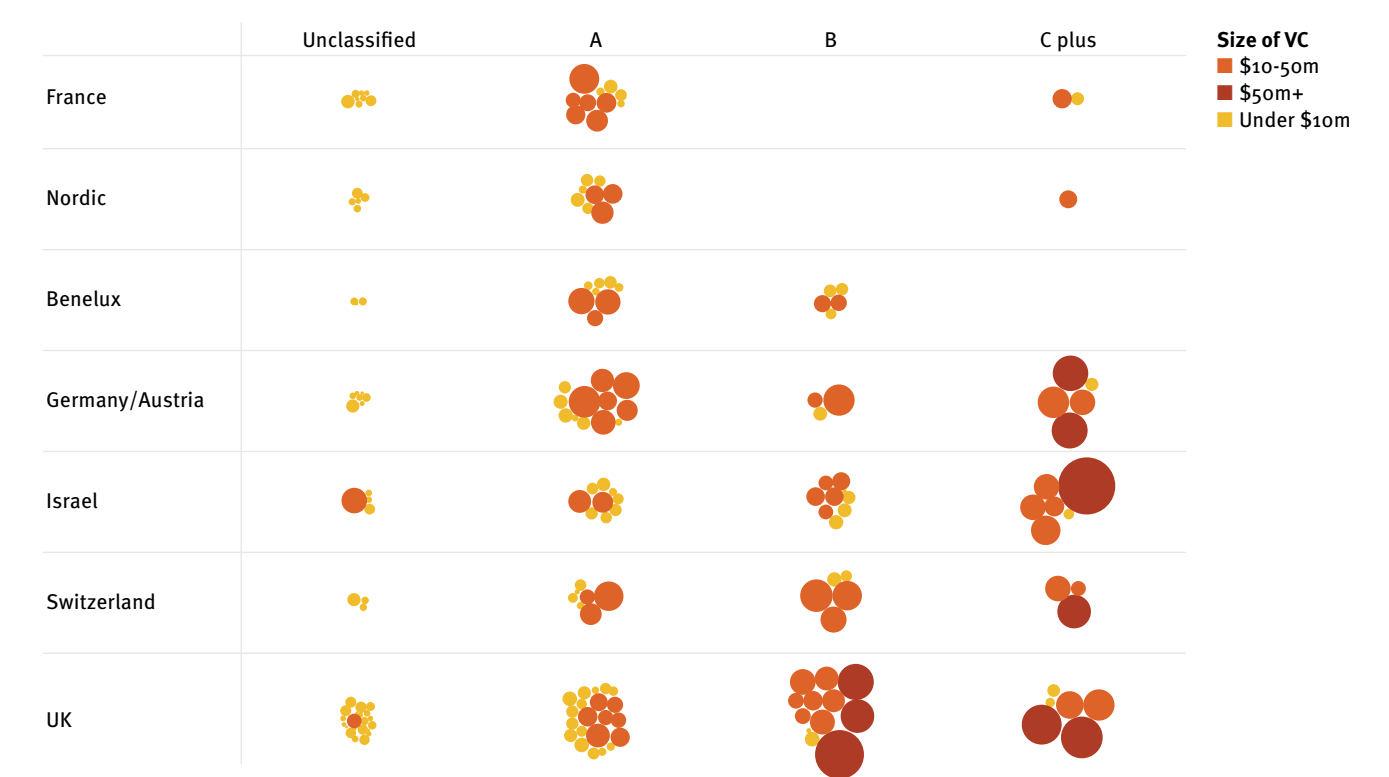
The pattern might not persist in 2018,

but it appears that in some territories, venture capitalists are keen to pass along early-stage risk to public market investors (which may include venture funds with options for public market holdings).

Funding Local Heroes

Much of the early-stage funding of European life science companies comes from funds that have a more regional, if not national focus. The most active European fund in 2017 was High-Tech Gruenderfounds, a public-private VC investment firm based in Bonn, Germany. It’s an early-stage seed investor, focused on high potential high-tech start-ups that are either German or have an independent subsidiary domiciled in the country. In 2017, High-Tech Gruenderfounds participated

Exhibit 3
Distribution Of Life Sciences VC (All Segments) Investment In European Territories



SOURCES: Strategic Transactions; Scrip | Pharma Intelligence, 2018

in nine different life science-focused investments.

While not exclusively focused on European opportunities, Forbion Capital Partners, a Dutch VC currently managing more than €700 million across six closed-end funds, is targeting EU companies primarily on EU targets, as well as Swiss, Norwegian and Canadian opportunities as, according to managing partner Sander Slootweg, comparable US companies have become too expensive. “We invest funds of €200 million on average and our current favorite sectors/areas are metabolic disorders, all viral vector approaches and neurodegenerative diseases,” he adds.

Indeed, the most active 13 venture capital groups in European life sciences were involved largely in early-stage investments: 60% of their investments (37 of 62 rounds) were in A rounds or earlier. The 62 investments in European rounds in 2017 were worth \$1,175 million, representing just over a quarter of the European Life Sciences VC total.

In many cases, European venture funds

have the European Investment Fund as a cornerstone investor and this can place some geographic restrictions on investment activity. Recent funds to get EIF include BGV III the third fund from Bio-Generation Ventures, which had a final closing €82 million. BGV III will focus on therapeutics, medical devices and diagnostics within Europe, in particular in Benelux and Germany.

BGV III, which also had backing from **Bristol-Myers Squibb Co.** and **Johnson & Johnson Innovation**, has already made five investments from the fund into German immuno-oncology company **Catalym GMBH**, and Dutch companies **Escalier Biosciences BV** (autoimmune diseases), **Scenic Biotech BV** (target discovery), **Varmx BV** (hematology) and **Mellon Medical BV** (vascular suturing).

There has been some concern that EIF backing for many European funds could have a negative impact on the ability of UK companies to access such money post-Brexit. While it is true that UK firms will find themselves chasing after smaller sums allocated to non-EU companies by

these funds, there is a confidence within boardrooms and among investors that quality companies need not be worried. EIF was one of the cornerstone investors in TVM’s TVM LSV, a fund created in 2005. “Conditions at that time were that a majority of the capital be invested in Europe. We do not see any impact post-Brexit on TVM LSV VI. We are currently investing from Fund VII and preparing to raise Fund VIII, both without participation of the EIF,” explains Hubert Birner, PhD, a managing partner at the German VC.

“We are looking for innovative companies in North America, Europe and Asia that have the potential for disruption in their sector; and who are looking for a VC who can help them accelerate. Which in our case means provide in-depth global industry insight and a closely knit network as well as the necessary, very specialized, operational experience in this industry. None of these are impacted by Brexit,” adds Birner.

Interestingly, proximity to investee companies is a major driver for many venture capitalists that are not constrained

Exhibit 4
Top Venture Capital Rounds In European Life Sciences 2017

COMPANY	LOCATION	FOCUS	DECLARED INVESTORS	ROUND	DATE	RAISED \$M
Roivant Sciences GmbH	Switzerland	Drug development	Softbank, Dexcel Pharma, previous undisclosed investors	ND	08/17	1,100
ADC Therapeutics SA	Switzerland	Oncology	Auven Therapeutics, Redmile Group, the Wild Family Office & AstraZeneca	D	10/17	200
Insightec Ltd	Israel	Medical Devices	Koch Disruptive Technologies, Elbit Imaging, York Capital, Exigent Capital Group, GE Healthcare, GEOC, & Meditech Advisors	E	01/18	150
Orchard Therapeutics Ltd	UK	Gene therapy	Baillie Gifford, ORI Capital, Temasek, Cowen Healthcare Investments, Juda Capital, Pavilion Capital, RTW Investments, Agent Capital, 4BIO Capital, F-Prime Capital & UCL Technology Fund	B		110
Autolus Ltd	UK	T cell therapies	Cormorant Asset Management, Nextech Invest, Syncona Ltd, Woodford Investment Management & Aris Bioscience	C		80
CellMedica Ltd	UK	Immunotherapy	Touchstone Innovations, Invesco Perpetual, & Woodford Investment Management	C	03/17	73
Iterm Therapeutics Ltd	Ireland	Antibiotics	Aris Bioscience, Pivotal bioVenture Partners, Advent Life Sciences, Domain Associates, Bay City Capital, Frazier Healthcare Partners, Canaan Partners, Sofinnova Ventures & New Leaf Venture Partners	C	05/17	65
Babylon Health	UK	AI-powered doctor app	None disclosed	B	04/17	60
Hookipa Biotech AG	Austria	Immunotherapy	Led by undisclosed US institutional investor, HBM Partners, Hillhouse Capital, Sirona Capital, Gilead Sciences, Sofinnova Partners, Forbion Capital Partners, Boehringer Ingelheim Venture Fund, Takeda Ventures & BioMedPartners	C	12/17	60
Immatics Biotechnologies GmbH	Germany	T cell therapies	dievini Hopp Biotech holding, Wellington Partners, AT Impf GmbH & Amgen	E	10/17	58
InflaRx NV	Germany	Inflammation	Bain Capital Life Sciences, Cormorant Asset Management & RA Capital	D	10/17	55
Xeltis AG	Switzerland	Medical Devices	Ysios Capital, LSP, Kurma Partners, VI Partners & private investors	C	11/17	52
Bicycle Therapeutics Ltd	UK	Bicyclic peptides	Vertex Ventures HC, Cambridge Innovation Capital, Longwood Fund, Novartis Venture Fund, SR One, SVLS & Atlas Venture	B	06/17	51

SOURCE: Strategic Transactions | Pharma Intelligence, 2018

Exhibit 5
Most Active Investors In European Life Sciences By Number Of Rounds

INVESTOR	# ROUNDS	% EU	BASED IN
High-Tech Gruenderfonds	12	100%	Germany
OrbiMed	9	27%	US
Novo AS	9	50%	Denmark
Life Sciences Partners	8	89%	Netherlands
Kurma Partners	8	100%	France
Sofinnova	7	41%	France/US
Boehringer Ingelheim Venture Fund	7	88%	Germany
Seventure Partners	7	88%	France
Johnson & Johnson Development Corp.	6	40%	US
Forbion Capital Partners	5	71%	Netherland
Ysios Capital	5	71%	Spain
Pontifax	5	83%	Israel
BioMedPartners	5	100%	Switzerland
Idinvest Partners	5	100%	France

SOURCES: Strategic Transactions; Scrip | Pharma Intelligence, 2018

by geographic restrictions. SVLS, the UK-based life sciences fund, is not restricted to the UK but tends to invest closer to home. “We have no predetermined allocation but invest mostly in UK deals because the management is stronger and the environment is more conducive,” notes SV Life Science’s managing partner Kate Bingham.

Nevertheless, Bingham will look further afield. Last fall, the Dementia Discovery Fund, created in 2015 with support from the UK government and five pharma companies to fund novel biology for neurodegenerative disorders and managed by SVLS, led the \$29.5 million in a Series D round in Alector LLC, a San Francisco-based company developing preclinical immunomodulatory therapies to treat neurodegenerative disorders including Alzheimer’s disease.

While acknowledging the European life sciences sector is an exciting environment with many excellent investment opportunities, Abingworth managing partner Tim

Haines remains agnostic to geography.

“We aim to invest in the best opportunities in life sciences, whether these are in the US or Europe. We invest primarily in therapeutics with an emphasis on early-stage deals. However, while there is no specific allocation between territories, our portfolios to date have been split roughly 60/40 between the US and Europe,” he says.

Although immuno-oncology is all the rage, and has attracted the most venture dollars, many VCs are looking to other sectors. Forbion invests funds of €200 million on average. SVLS’ Bingham adds, “For IO deals, we need to believe we can generate persuasive, differentiated profiles given how busy the field has become.” She prefers to focus on immunology and CNS, especially dementia.

Going Global

While much of the money put to work in European life sciences is linked to regional and local funds, interest from

global investors such as OrbiMed confirms that quality opportunities in Europe can attract funds. “While the majority of our investments are in the US we see a lot of exciting European companies that don’t have as many investor dollars chasing them. Indeed, there can be more opportunity to work with companies in Europe than say Boston or San Francisco where there are lots of investors closing deals,” Carl L. Gordon, PhD, general partner and co-head of Global Private Equity at OrbiMed, tells *In Vivo*.

Even though OrbiMed does not have an office in Europe nor a specific allocation for European businesses, according to our data, it ranked just below the largely-German seed funder, High-Tech Gruenderfonds, for investor activity in the region in 2017. OrbiMed participated in 33 life sciences venture investments in 2017, nine of which were in European businesses. But OrbiMed is geographically agnostic, so European businesses must compete against US opportunities from OrbiMed’s current \$1 billion global VC fund, OrbiMed Private Investments VII.

“Our main focus is on companies developing therapies that are truly novel in their approaches at any stage in the development cycle from preclinical assets through to ready-for-market drugs. To a lesser extent, we will look at diagnostics, digital health and medical devices but at a later stage,” Carter Neild, a general partner at OrbiMed, adds.

OrbiMed has two venture partners with close ties to Europe – Iain Dukes, DPhil, who was previously as senior vice president, business development and licensing at MSD, and Klaus Veitinger, MD, PhD, who was on the executive board of Schwarz Pharma AG and CEO of Schwarz Pharma Inc. These industry veterans will take board positions on European companies that OrbiMed invests in as well as provide them operational decision support.

Not surprisingly, cancer, neurodegenerative and rare diseases top OrbiMed’s wish list.

Israel Flies The Banner For Medtech

Medtech investment in the European Union has largely ground to a halt probably because of the substantial tightening

Exhibit 6
Most Active Investors In European Life Science A, B And C Rounds By Total Average Investment Contribution*

INVESTOR	EU \$M	# ROUNDS EU	BASE
Life Sciences Partners	48.93	8	Netherlands
Touchstone Innovations	43.31	4	UK
Woodford Investment Management	40.4	3	UK
Sofinnova	40.23	7	France/US
Ysios Capital	39.04	5	Spain
Novo AS	36.47	9	Denmark
Kurma Partners	34.29	8	France
Boehringer Ingelheim Venture Fund	33.69	7	Germany
OrbiMed	31.44	9	US
Forbion Capital Partners	30.98	5	Netherlands
F-Prime Capital Partners	29.47	3	US
Abingworth Management	29.18	2	UK
Invesco Ltd.	28.13	2	UK
TVM Capital	28	2	Germany
Syncona Partners LLP	27.25	2	UK
Arix Bioscience	27.22	4	UK
Novartis Venture Fund	24.85	4	Switzerland
Seventure Partners	24.67	7	France
Versant Ventures	20.18	2	US
GIMV	19.69	2	Belgium
New Enterprise Associates	19.25	2	US
High-Tech Gruenderfonds	18.1	12	Germany

*Average investment contribution is obtained by dividing each investment by the number of investors involved. Adding together all the average contributions from a given investor yields the total average investment size.

SOURCES: Strategic Transactions; Scrip | Pharma Intelligence, 2018

of regulatory constraints, but continues apace in Israel.

Exhibit 7 illustrates that in 2017, medtech companies from Israel (~8.5 million people) attracted almost as much

venture investment - \$285 million - at all stages in the financing process as companies across the whole of the rest of Europe (\$348 million; ~525 million people).

Medtech investments accounted for

over half of all life sciences venture capital going into Israel (\$285 million out of \$495 million). Half of the Israeli total (\$150 million) went to **Insightec Ltd.**, which is developing magnetic resonance imaging-guided focused ultrasound surgery, in what is believed to be the company's last pre-IPO venture round.

To tap into such opportunities, OrbiMed established a dedicated Israeli fund although its focus is evolving. Having initially focused on medtech opportunities, OrbiMed's Gordon notes that the firm is seeing opportunities in emerging biotherapeutics. "We set up the Israeli fund because we identified a lot of opportunities in the Israeli medtech space but biotech is emerging there. However, our investments in the Israeli therapeutics space tend to be much earlier than we would do in either the US or Europe," he adds.

Medtech, however, is losing some of its luster. Forbion Capital, for example, used to put about 30% of its funds into medtech companies but has now downgraded that allocation to about 15%. "Medtech in our view has become less attractive because of a more restrictive regulatory environment in Europe and more cumbersome reimbursement procedures. In addition, public markets in general have been less receptive for medtech stories, compared with biopharma and there are fewer buyers in this space left, after massive consolidation has occurred in the past decade, so acquirers can afford to wait a little longer. This forces our companies typically into early commercialization activities, with limited means and typically only one product to sell, this is not very economical," notes Forbion's Sloodweg.

Growth Capital Opportunities

Getting access to the large boluses of cash companies need to build their businesses remains a challenge for European companies but there are a growing number of options. "Funding always remains a concern. Anecdotally we know that compared with US CEOs, European CEOs spend more time raising their rounds -which means they must be distracted to some extent from other tasks. The funding challenge is specifically at the B round when choice of public, M&A, large B round, etc. is being made," explains Nooman Haque, a

Exhibit 7
Medtech Investment In 2017: Europe Vs. Israel



SOURCES: Strategic Transactions; Scrip | Pharma Intelligence, 2018

managing director at Silicon Valley Bank.

Where to go public is always a challenge for European life sciences companies. Although there has been an uptick in European IPOs in recent years, companies listing on European exchanges face a number of challenges. First, the amount of money that can be raised in Europe is nowhere the same level that is achievable in the US. Second, analyst coverage in Europe is both limited in terms of quantity and quality. Third, and probably most important long term, liquidity and access to substantial follow on financing is a major stumbling block.

While European companies can raise equivalent sums to US firms in the early years, the amount of money available subsequently is much lower in Europe. This creates opportunities for investment firms to create specific growth vehicles.

Medicxi Ventures last year, with support from Verily Life Sciences, a subsidiary of Google parent company Alphabet, Novar-

tis and the European Investment Fund, established Medicxi Growth 1 - a \$300 million fund focused on investments in emerging companies with drug candidates in Phase IIb and beyond.

From MG1, Medicxi intends to lead syndicates, putting in €10-€25 million per company, with about 80% earmarked for European companies and the remainder going into US opportunities. To date, MG1 has anchored the \$96.8 million IPO of ObsEva SA, a Switzerland-based women's health company, and invested in the Cleveland, OH-based diabetes company Diasome Pharmaceuticals Inc.

OrbiMed is already providing substantial growth capital through a dedicated \$1 billion fund focused on structured finance and royalty-based financing, OrbiMed Royalty Opportunities II, explains Matthew Rizzo, a partner in OrbiMed's credit business. "We focus on later-stage opportunities, for example in compa-

nies that are building out commercial infrastructures, making acquisitions, or in-licensing products. Investments can be substantial, upwards of \$150 million, ideally with commercial-stage innovative products and strong intellectual property."

One European company to benefit from such support is the Dutch biopharma company **Pharming BV**. "We saw an interesting opportunity in a rare disease-focused company with an under-appreciated asset that needed a minimally-dilutive financing solution," he says. In 2017, OrbiMed provided Pharming with a four-year \$100 million senior secured debt facility to refinance debt on more favorable terms to redeem a total of €35.9 million of amortizing convertible bonds and refinance \$40 million of senior debt. ▶

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Comments:

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