

Fueling life sciences through transformative transactions

LOCUST WALK 2018 ANNUAL REPORT

Global Trends in BioPharma Transactions

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FINDINGS AND PREDICTIONS

Introduction

Locust Walk is a global life science transaction firm. Our integrated team-based approach across capabilities, geographies, and industry segments delivers the right products, the right partners, and the most attractive sources of capital to get the right deals done for biopharma and medtech companies.

Each quarter, Locust Walk deal team members compile key statistics and trends on strategic transactions and financings. Our *2018 Annual Report: Global Trends in BioPharma Transactions* applies the latest data to analyze current activities in the life sciences deal landscape.

In this report you can find an overview and analysis of the following across the biopharma market in the US, Europe, and Asia (Japan and China):

- Key performance indicators for the life science market
- IPO and private financing activity and performance
- Deal activity for strategic partnership and M&A
- A look ahead and our predictions of the future

Summary of BioPharma Findings and Predictions (1/2)

US

- Biopharma continues to draw significant investment dollars, despite a broader market sell-off that sent the Nasdaq Biotechnology Index to its lowest levels since July 2018
- Biopharma IPO market remained robust in Q4, with an increase in total amount raised despite a lower volume compared to Q3, led by Moderna, which had the largest IPO in biotech history
- 2018 private financings outpaced 2017 in both amount raised and volume of transactions, showing a steady pool of capital remains for early-stage biopharma investments
- Q4 M&A deal volume and aggregate deal value decreased from Q3, but mega deals in 1H 2018, such as the acquisition of Shire by Takeda still made 2018 a strong year for biopharma M&A
- Licensing deal volume and deal value increased in Q4 from Q3 as uncertainties began to emerge about the sustainability of public markets
- LW anticipates an increase in licensing and M&A activity in 2019 as public/private financing markets remain robust but likely lower than record financings of 2018

Summary of BioPharma Findings and Predictions (2/2)

Europe

- 2018 EU VC investment aggregate volume and value is the highest of any year in the last 8 years
- Given the uncertainty of the European public markets, Locust Walk expects to see the continued strength in EU VC, other private investment, and deal making to support growth for 2019
- Locust Walk expects pharma companies to increasingly look to the EU to acquire interesting platform or therapeutics as the science is strong and valuations are attractive for buyers

Japan

- Volatility of shares of the top 40 Japanese biotech companies in 2018 was much greater than 2017 with overall weak performance since Q2, seeing a downward trend, ending -19% YoY in 2018
- The volume of Japan licensing deals with announced size of >\$10M in 2018 hit record highs since 2008; Takeda's acquisition of Shire was the biggest deal across all M&A deal history by a Japanese company
- Expect more in-licensing activities by Japan pharma due to emphasis on open innovation and pipeline shortage, especially from mid-tier pharma

China

- In-licensing deal volume has significantly increased with substantial front-end economics
- 2018 was a weak year for Chinese public pharmaceutical companies partially due to US-China trade war and the enormous drug price cuts in recent tenders
- Expect continued interest in Hong Kong Exchange biotech listing expanding beyond Chinese ventures and further in-licensing activities by both traditional and emerging biopharma companies

BIOPHARMA UNITED STATES

BioPharma United States Overview (1/2)

Despite biotech indices falling in Q4, 2018 was a boom year in biopharma IPOs with 70 companies filing to go public on US exchanges this year

- Despite a decline in Q4 IPO volume, Q4 had increased total offering amount due to two of the biggest IPOs in biotech history
 - Highest valued offerings were concentrated in technology platforms such as mRNA, CAR-T and gene therapy
- 2018 private financings broke the record for amount raised by over \$3B and volume by >30 deals
- Companies raised private funds at all stages in Q4, which in light of the volatile public market, confirmed the strength of the market for private biopharma financing
 - Many deals were concentrated in the immuno-oncology and gene therapy spaces, however companies across a broad range of therapeutic areas secured private funding

BioPharma United States Overview (2/2)

M&A activity set a record for deal volume, while the aggregate M&A deal value decreased further from the highs of 2015-2016

- Despite decline in Q4 deal values and deal amount, the 2018 M&A average deal value and deal amount surpassed 2017, largely due to the abundance of smaller deals and a few mega deals in 1H 2018 (Shire/Takeda and Tesaro/GSK)

2018 licensing volume and licensing deal value increased from 2017

- Q4 licensing deals increased from Q3, reinforcing licensing remains a key source of non-dilutive financing

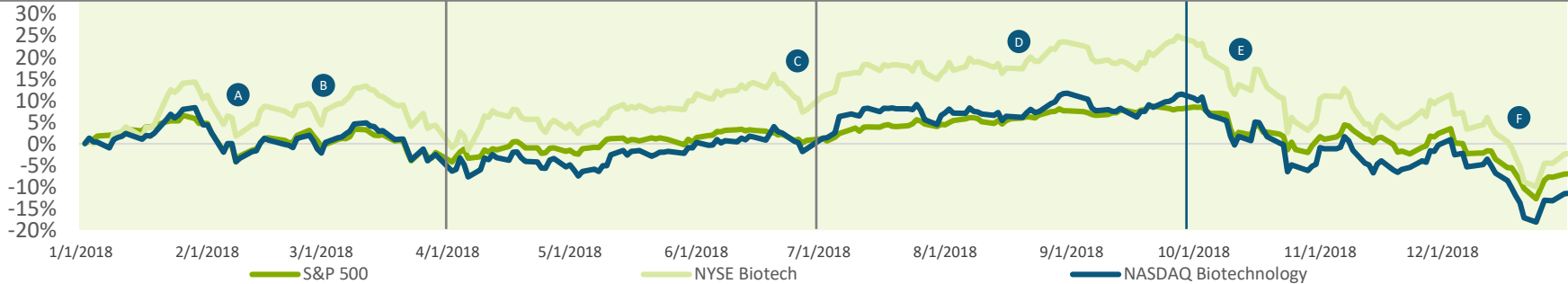
Locust Walk anticipates 2019 to be a “normalization” year with the ratio of financings to M&A and licensing transactions to be more in line with traditional trends

- Decreasing certainty of IPOs could reduce financing activity and/or lower financing valuations, which should lead to an increase in non-dilutive transactions (licensing) and M&A as they become more attractive options
- Life sciences VCs and PEs raised larger new funds in 2018, indicating there is considerable capital to be deployed in 2019

Public biopharma indices suffered a dramatic swing at the end of 2018

Performance of Key Biopharma Indices

	Q1 2018	Q2 2018	Q3 2018	Q4 2018
ΔS&P%	(2.04%)	5.29%	7.20%	(14%)
ΔNBI%	(2.51%)	7.20%	13.24%	(22%)
ΔNYSE BTK%	4.21%	10.91%	11.06%	(21%)



2018 Return

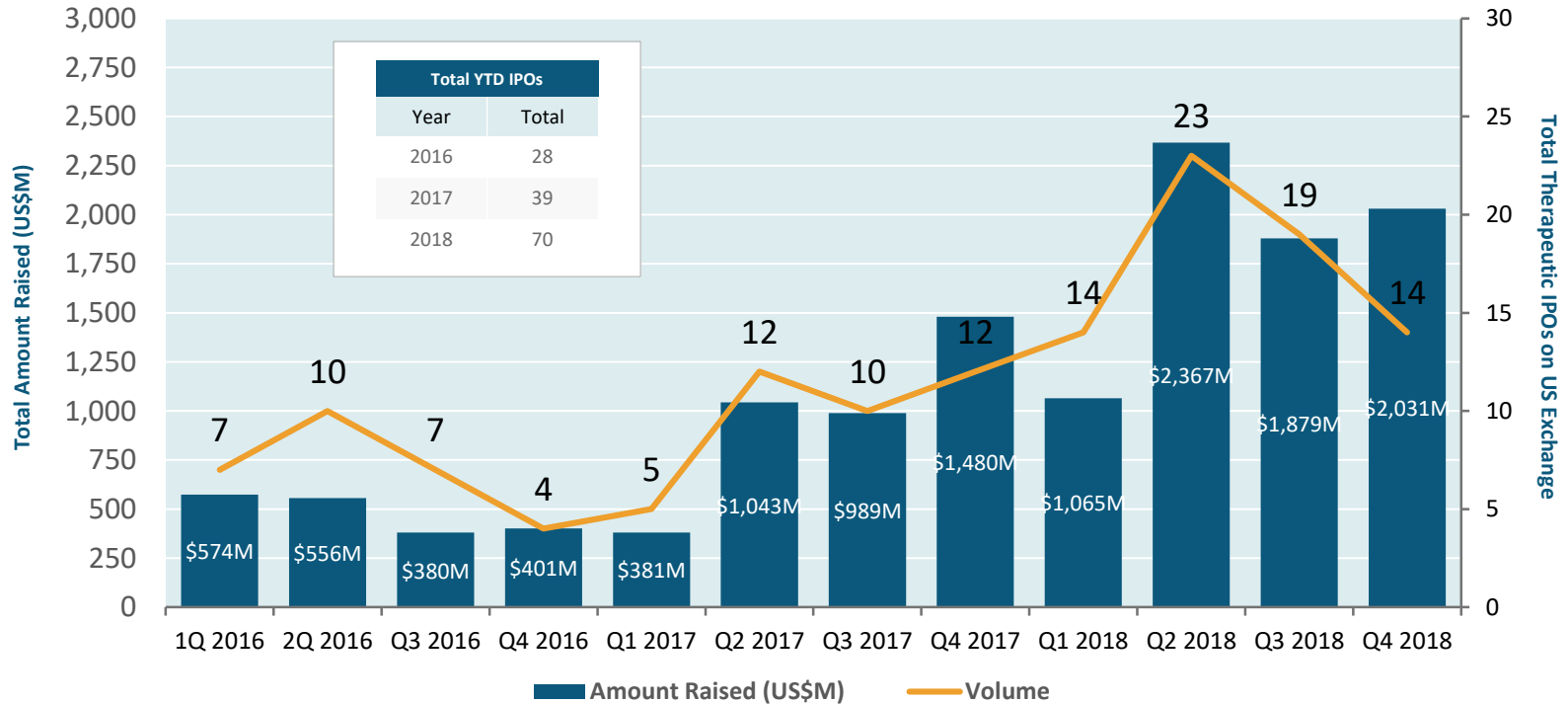
S&P: (7.01%)
 NYSE BTK: (2.34%)
 NBI: (11.54%)

- Key Event**
- A Dow plunges 1,597 points as investor pessimism rapidly rises due to the sell-off in the bond market
 - B NASDAQ rises 1.8% after jobs report suggests US added 313,000 jobs in February
 - C Concern over international trade negatively contributes to the rise of investor pessimism
 - D Biotech stocks rise after 9 FDA approvals in 22 days
 - E Federal Reserve Chairman comments around future rate hikes sharper than expected
 - F Stocks faced steep decline following interest rate increases, political tensions, and market turmoil

SOURCE: Locust Walk Analytics, Yahoo Finance

2018 was a prolific year for biotech IPOs, with IPO volume surpassing that of 2017 and 2016 combined

Number of Biopharma IPOs and Aggregate Total Raised By Quarter



SOURCE: EDGAR Company Filings, Yahoo Finance, Global Data, Pitchbook




While 14 biopharma companies filed for IPOs in 4Q18, market volatility led many to downsize their offerings

Q4 US IPOs									
Biopharma Issuer	Ticker	Therapeutic Area	Lead Phase	Deal Date	Price Range	Offering Price	Total Raise (M)	Price Change IPO to 1/7	Market Cap (M) **
Harpoon Therapeutics* South San Francisco, CA	HARP NASDAQ	Immuno-oncology	Phase 1 Ongoing	12/27/2018	N/A	N/A	\$86*	N/A	N/A
Gossamer Bio* San Diego, CA	GOSS NASDAQ	Immunology	Phase 2b Ongoing	12/21/2018	N/A	N/A	\$265*	N/A	N/A
Synthorx La Jolla, CA	THOR NASDAQ	Oncology, autoimmune diseases	Preclinical Ongoing	12/7/2018	\$10 – \$12	\$11.00 Middle	\$131	12.9%	\$478
Moderna Therapeutics Cambridge, MA	MRNA NASDAQ	mRNA therapeutics in oncology	Phase 2 Ready	12/6/2018	\$22 – \$24	\$23.00 Middle	\$604	(30.6%)	\$5,766
Eton Pharmaceuticals Deerpark, IL	ETON NASDAQ	Specialty pharma in liquid products	FDA Filing	11/13/2018	\$5 – \$7	\$6.00 Middle	\$22	(4.2%)	\$105
Orchard Therapeutics London, UK	ORTX NASDAQ	Gene therapy for genetic diseases	Marketed	10/31/2018	\$14 – \$16	\$14.00 Low	\$200	(7.5%)	\$1,349
Twist Bioscience San Francisco, CA	TWST NASDAQ	Synthetic biology manufacturer	Marketed	10/31/2018	\$14 – \$16	\$14.00 Low	\$70	(77.6%)	\$779
LogicBio Therapeutics Cambridge, MA	LOGC NASDAQ	Gene Therapy	Pre-clinical	10/19/2018	\$12 – \$14	\$10.00 Low	\$70	(2.9%)	\$224
Osmotica Pharmaceutical Marietta, GA	OSMT NASDAQ	Neurology	Marketed	10/18/2018	\$14 – \$16	\$7.00 Low	\$47	(13.9)	\$423
PhaseBio Malvern, PA	PHAS NASDAQ	Orphan, cardiopulmonary conditions	Phase 2b Ongoing	10/18/2018	\$12 – \$14	\$5.00 Low	\$46	(38.2%)	\$80
Equillum La Jolla, CA	EQ NASDAQ	Autoimmune disorders	Phase 1b Ready	10/12/2018	\$14 – \$16	\$14.00 Low	\$65	(43.1%)	\$159
Allogene Therapeutics South San Francisco, CA	ALLO NASDAQ	Immuno-oncology	Phase 1 Ongoing	10/11/2018	\$16 – \$18	\$18.00 High	\$324	22.4%	\$3,330
Hoth Therapeutics* Cincinnati, OH	HOTH NASDAQ	Skin conditions	Preclinical	10/10/2018	N/A	N/A	\$7*	N/A	N/A
Kodiak Sciences Palo Alto, CA	KOD NASDAQ	Retinal Diseases	Phase 2 Ready	10/04/2018	\$13 – \$15	\$10.00 Low	\$90	(29.0%)	\$287

* IPO filed, but not completed; ** Market cap as of 1/7/2019

SOURCE: Locust Walk Analytics, EDGAR Company Filings, Yahoo Finance, Pitchbook

4Q18 saw two of the biggest IPOs in biopharma history, as well as a large offering by an EU biopharma

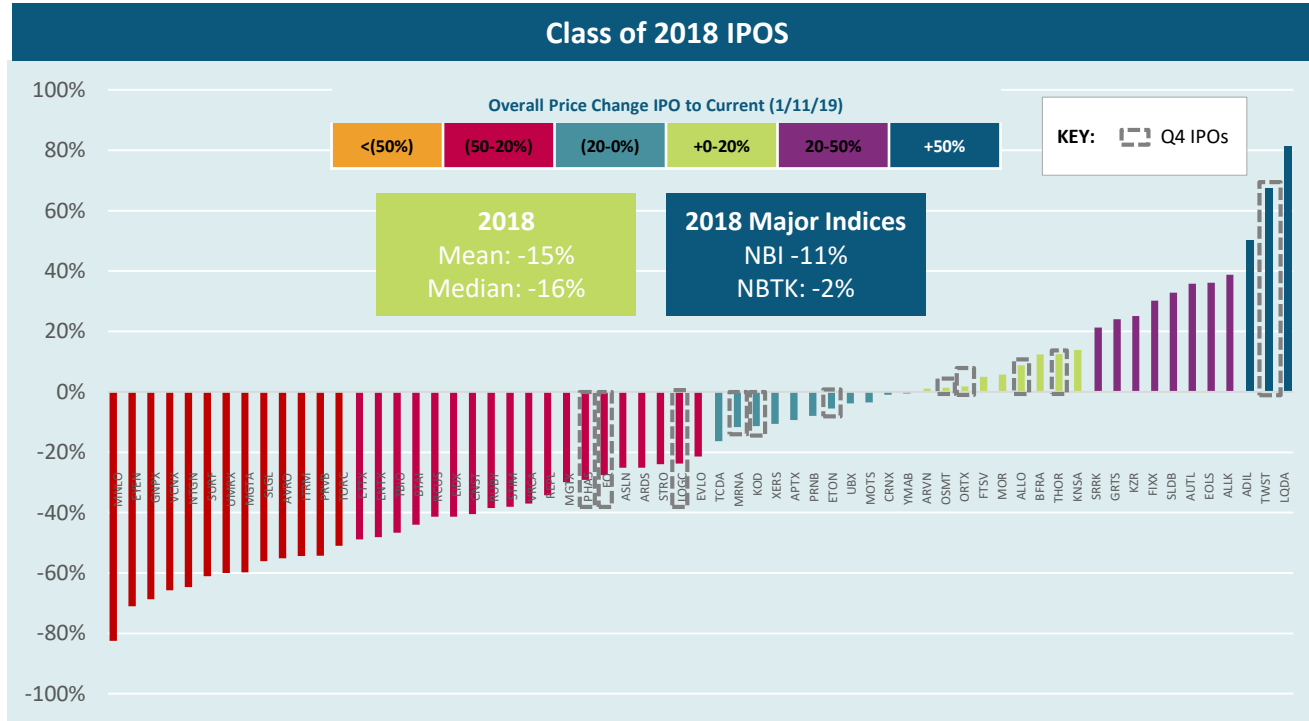
			
Summary	Developer of messenger RNA therapeutics and for inherited genetic disorders, oncology and hemophilic & blood factors	Developer of allogenic chimeric antigen receptor T-cell (CART) therapy for oncology	Developer of ex vivo gene therapeutics for rare, life-threatening genetic disorders
Pipeline	<ul style="list-style-type: none"> • 21 programs in phase 1 & 2 • Lead: phase 2 AZD8601 for myocardial ischemia, partnered with AstraZeneca 	<ul style="list-style-type: none"> • 8 programs in preclinical & phase 1 • Lead: phase 2 UCART19 for acute lymphoblastic leukemia 	<ul style="list-style-type: none"> • 8 programs in clinical development with other preclinical programs • Lead: EU-approved strimvelis for adenosine deaminase severe combined immunodeficiency
Amount Raised	\$604M	\$324M	\$200M
Market Cap (1/7)	\$5,766M	\$3,330M	\$1,349M

Wave of biotech IPOs have increasingly favored companies with wide-ranging biological platforms with multiple applications that give investors more opportunities for success

SOURCE: Locust Walk Analytics, EDGAR Company Filings, Yahoo Finance, Pitchbook

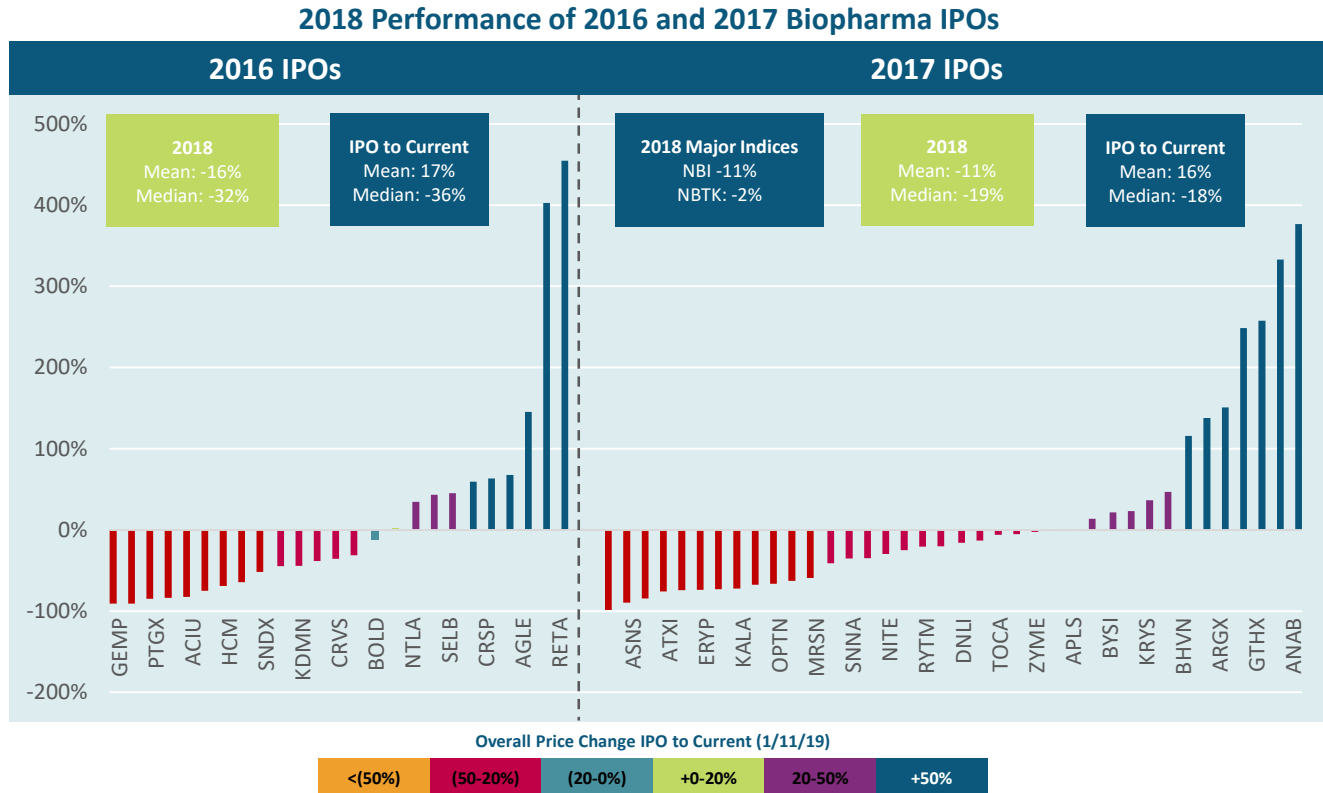
2018 IPO volume soared, but their stocks underperformed when compared to major biotech indices

Current Performance of 2018 Biopharma IPOs



SOURCE: Locust Walk Analytics, Data provided for free by IEX, View IEX's Terms of Use

Class of 2017 IPOs reflected overall market trends while the class of 2016 IPOs have severely underperformed



SOURCE: Locust Walk Analytics, Data provided for free by IEX, View IEX's Terms of Use

BioPharma United States Financing (1/2)

2018 private financings set a record for amount raised by >\$3B and volume of transactions by >30 deals

Number of Series C rounds increased by 78% as compared to 2017, signaling that later-stage companies continue to have access to private capital

- Amount raised in Series C also increased 117% from 2017, providing further evidence of later-stage biotech companies accessing unprecedented amounts of capital as new investor types enter the asset class

Number of Series A rounds decreased by 5% from 2017, but the total amount raised in Series A rounds increased by 35%

- Over \$4.6B raised in Series A rounds indicates the potential for companies to secure larger amounts of funding in earlier rounds
- Series A rounds accounted for over 33% of total dollars raised, suggesting strong investor appetite for early-stage biotech and the continued expansion of the company creation-focused VC business model

BioPharma United States Financing (2/2)

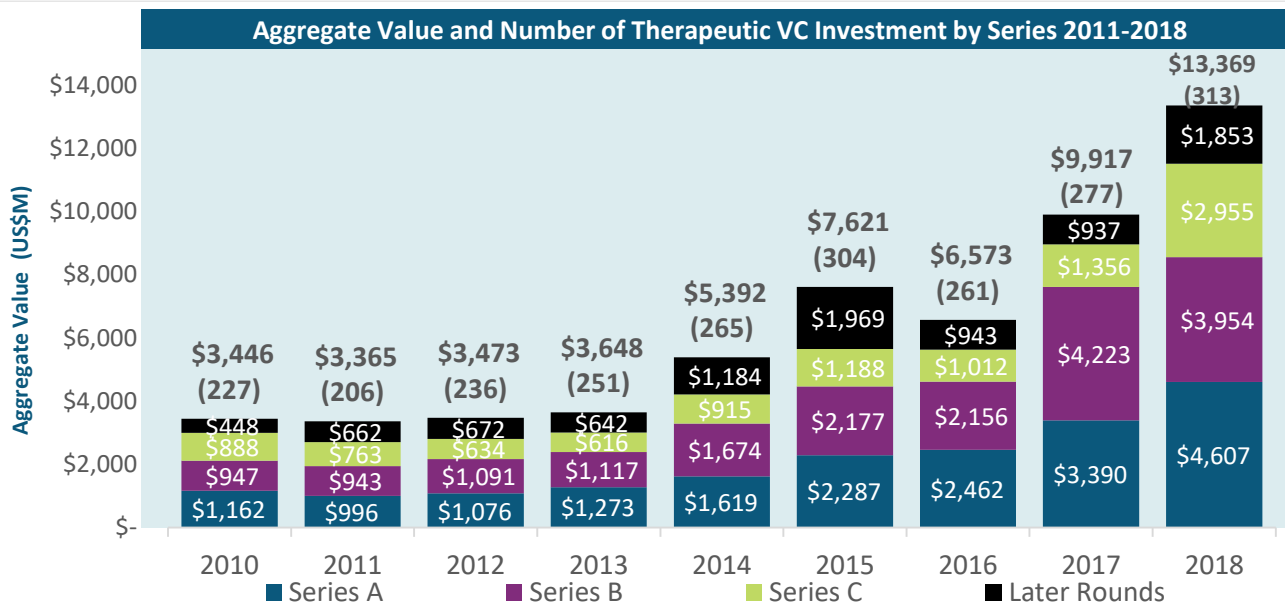
Moderna raised the most capital in 2018 with a \$500M crossover raise before going public with a record-breaking \$600M IPO

- In Q4, Mirum Pharmaceuticals raised the most money with a \$120M Series A raise led by New Enterprise Associates to advance their therapies for cholestatic liver diseases

Public market volatility in Q4 did not lead to any significant decrease in private financing deals in the quarter, but it is yet to be seen how any continued volatility will affect 2019 Q1 deals

- If the current prolonged IPO window is shutting, Locust Walk believes the “canary in the coal mine” will be a drop in the number of crossover rounds in Q1
- Earlier stage financings not targeting a near term IPO are less likely to be affected by the volatility









2018 breaks previous records for private biopharma financing for both volume and aggregate deal value



Deals (#)	2010	2011	2012	2013	2014	2015	2016	2017	2018
A	112	92	116	120	117	152	134	144	138
B	58	58	65	77	88	79	73	85	95
C	35	29	28	29	34	44	33	32	57
D & Later	22	27	27	25	26	29	21	16	23
Total	227	206	236	251	265	304	261	277	313

SOURCE: Locust Walk analytics, Pitchbook; Methodology: All US series A, B, C, D, and later investments; therapeutics include drug delivery, drug discovery, pharmaceuticals, and select biotechnology companies; tools, devices, and diagnostics excluded

Large amounts of capital were raised in early rounds across broad sweep of therapeutic areas in Q4 2018

High-Value Investment Rounds					
Company	Series	Raised (\$M)	Lead Investor	Therapeutic Area	Background
Mirum Pharmaceuticals	A	120		<ul style="list-style-type: none"> Gastrointestinal 	<ul style="list-style-type: none"> Mirum Pharmaceuticals is hitting the ground running with a phase III-ready therapy licensed from Shire for debilitating liver diseases, Alagille syndrome (ALGS) and progressive familial intrahepatic cholestasis (PFIC)
	B	93		<ul style="list-style-type: none"> Immuno-oncology 	<ul style="list-style-type: none"> NextCure is developing a preclinical pipeline of immuno-oncology therapies
	B	90		<ul style="list-style-type: none"> CNS 	<ul style="list-style-type: none"> Stoke Therapeutics is focused on developing antisense oligonucleotide medicines for Dravet Syndrome and other severe genetic diseases, with the goal of being in the clinic by early 2020
KALLYOPE	B	87		<ul style="list-style-type: none"> CNS and metabolic disorders 	<ul style="list-style-type: none"> Kallyope is advancing a portfolio of discovery-stage therapies that leverage the gut-brain axis to treat a range of metabolic and CNS disorders
	B	80		<ul style="list-style-type: none"> Oncology and gastrointestinal 	<ul style="list-style-type: none"> Terns is advancing small molecules to treat NASH and oncology
	B	77	Undisclosed	<ul style="list-style-type: none"> Immuno-oncology and autoimmune diseases 	<ul style="list-style-type: none"> Celularity uses stems cells to create transformative therapies for conditions from cancer to Crohn's disease

SOURCE: Locust Walk analytics, Pitchbook

BioPharma United States Transactions (1/2)

2018 licensing deal volume and deal value increased from 2017

- Increase in licensing deal value likely tied, in part, to availability of capital for financing alternatives that provided licensors more optionality to drive higher licensing deal economics
- The volume and value of Q4 licensing deals increased from Q3 as fewer companies completed IPOs as compared to earlier in the year and companies were more willing to obtain non-dilutive capital

2018 M&A deal volume and deal value increased from 2017

- The higher deal value of 2018 was largely driven by the mega deals of 1H 2018, including the Takeda/Shire \$62B deal and then later by the \$5.1B GSK/Tesaro acquisition
- Q4 M&A deal volume and deal value decreased from Q3, as likely acquirer's stocks were hit hard by public market turmoil, however the abundance of mega deals of 1H 2018 still made 2018 a strong year for biopharma M&A

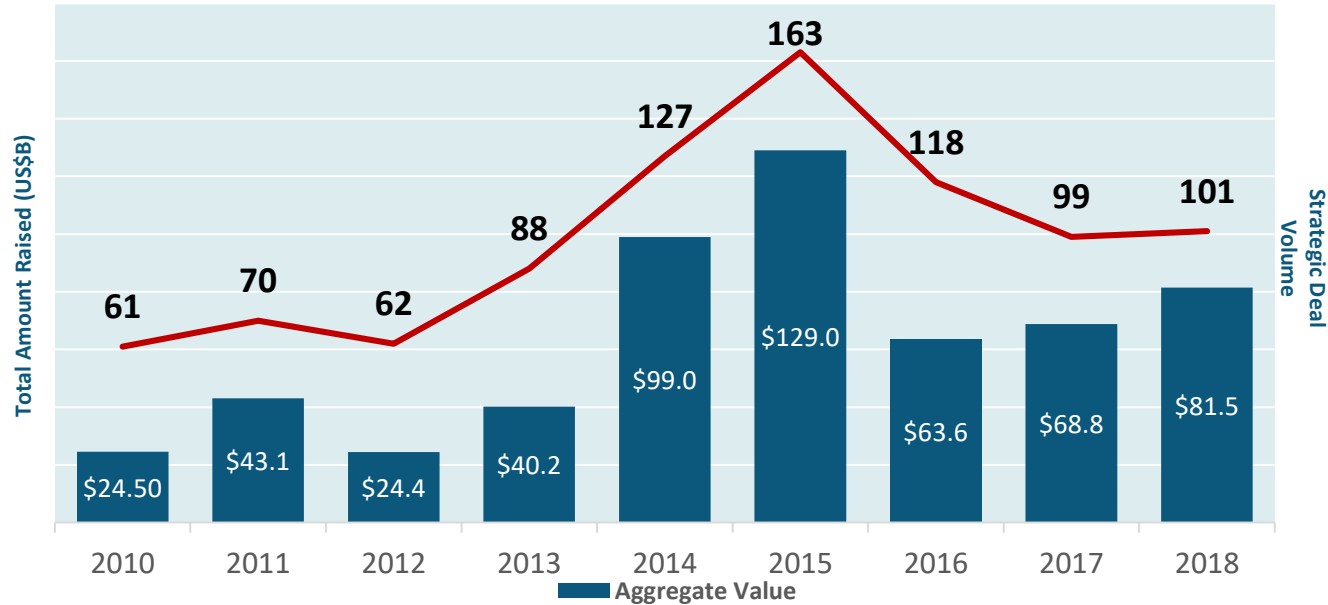
BioPharma United States Transactions (2/2)

Locust Walk anticipates an exciting and active 2019 for biopharma strategic partnering and M&A deal making due to potential continued volatility in public markets and large cash balances at several potential acquirers

- Companies funded in 2015-17 are beginning to achieve value inflection points in innovative technologies and become attractive as targets for licensing or acquisition
- Buyers continue to have access to capital to fund transactions and the need for further pipeline expansion
- If access to public or private capital begins to slow and valuations lower as stocks underperform, partnering and M&A become more attractive sources of investor returns

2018 deal volume and value surpassed 2017, while still trailing behind the highs of 2014-2015

US and WW Biopharma Licensing Deals (>\$50M Total Deal Size)

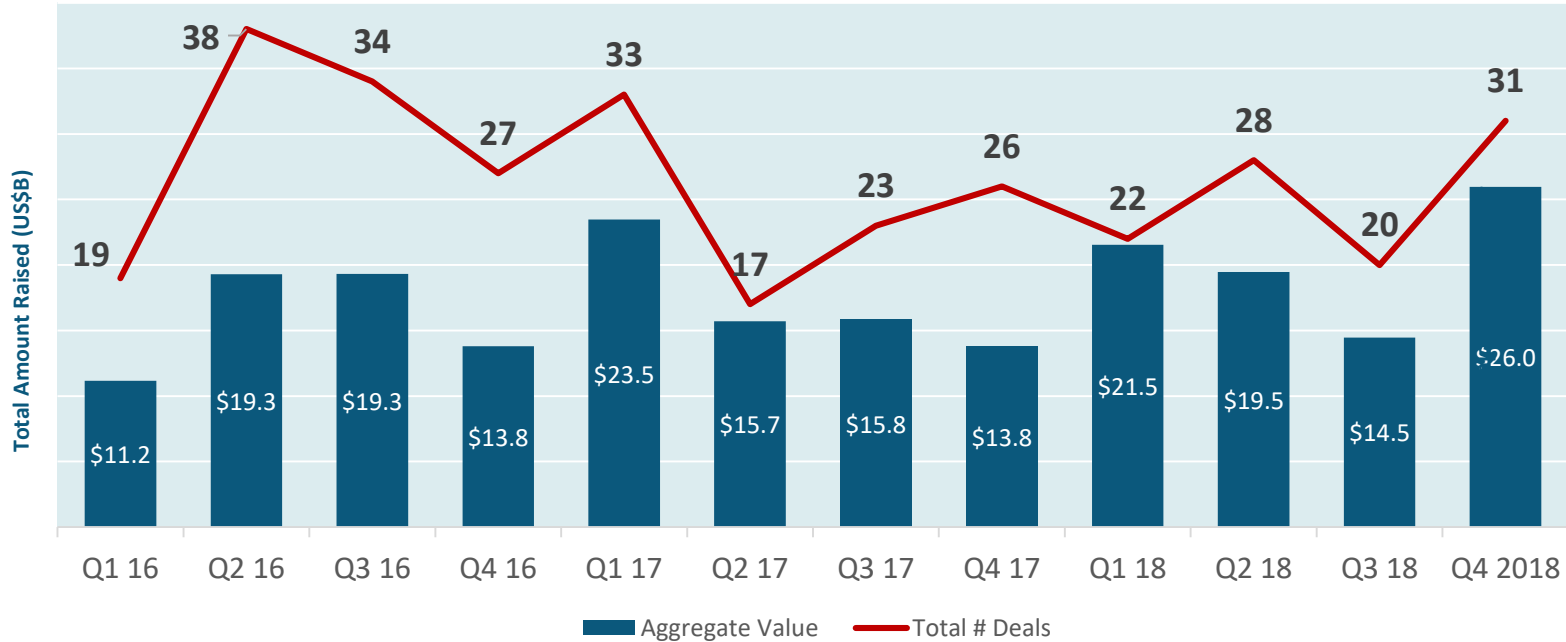


	2010	2011	2012	2013	2014	2015	2016	2017	2018
Avg Deal Size	\$402M	\$615M	\$394M	\$456M	\$779M	\$791M	\$539M	\$695M	\$760M

SOURCE: Locust Walk analytics, BioSciDB; *Locust Walk has altered methodology beginning Q3 2017; includes WW and US licensing deals; ex-US regional deals are excluded

Q4 2018 licensing volume and licensing deal value increased from Q3

US and WW Biopharma Licensing Deals (>\$50M Total Deal Size)



SOURCE: Locust Walk analytics, BioSciDB; *Locust Walk has altered methodology beginning Q3 2017; includes WW and US licensing deals; ex-US regional deals are excluded

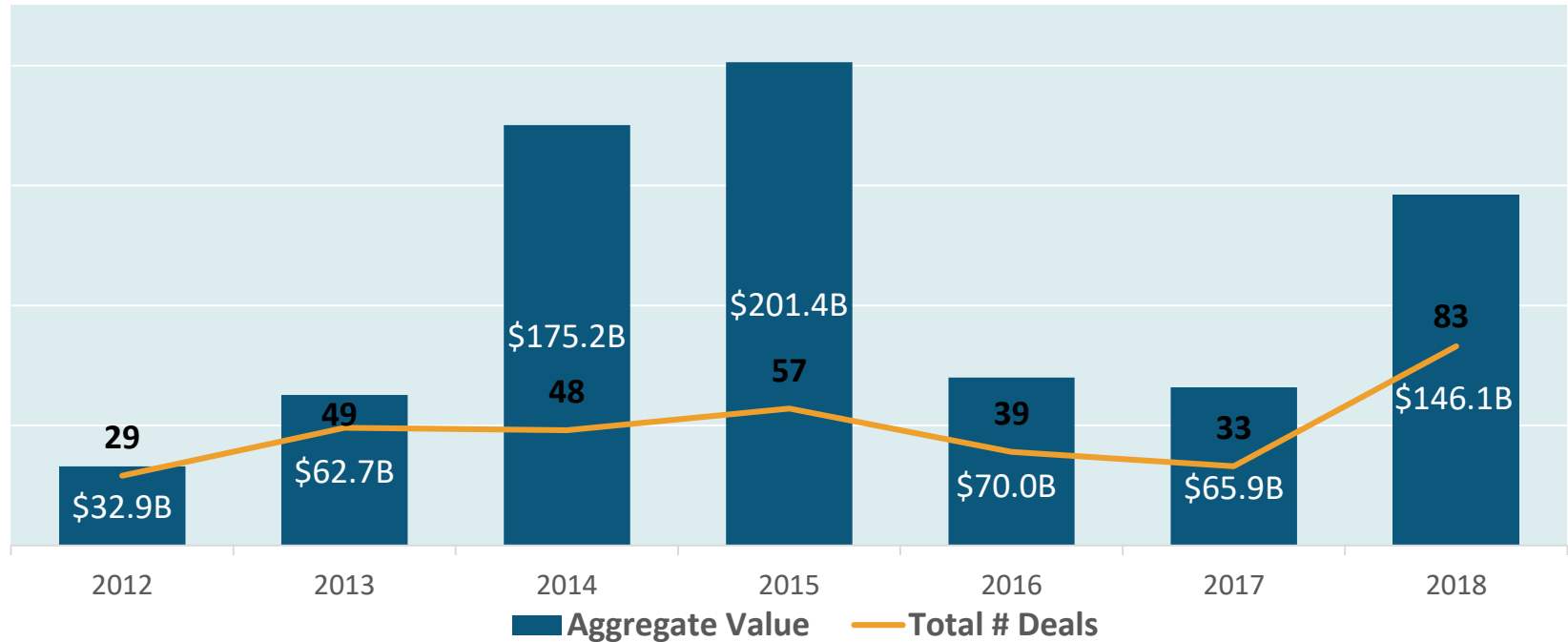
Q4 licensing deals heavily concentrated in early-stage assets

Q4 Licensing Deals								
Licensee	Licensor	Date	Stage	Total Deal Size (\$M)	Upfront (\$M)	Milestones (\$M)	Therapeutic Area	Deal Background
Johnson & Johnson	Arrowhead Pharmaceuticals	Oct-2018	Phase I	3,750	250	3,500	Infectious disease	<ul style="list-style-type: none"> Exclusive WW license to Arrowhead's ARO-HBV program and option to collaborate on three new targets
Lilly	AC Immune	Dec-2018	Preclinical	1,908	131	1,777	CNS	<ul style="list-style-type: none"> WW commercialization rights for tau aggregation inhibitors for Alzheimer's disease
Gilead	Agenus	Dec-2018	Preclinical	1,850	150	1,700	Oncology	<ul style="list-style-type: none"> Exclusive license to AGEN1423 I/O bispecific antibody and option to license two early-stage I/O therapies
Janssen / J & J	Argenx	Dec-2018	Phase II	1,800	500	1,300	Oncology	<ul style="list-style-type: none"> Exclusive license to Cusatuzumab, an anti-CD70 SIMPLE antibody for hematological malignancies including AML & MDS
Gilead	Tango Therapeutics	Oct-2018	Discovery	1,750	50	1,700	Oncology	<ul style="list-style-type: none"> Worldwide rights on up to 5 I/O targets emerging from Tango's functional genomics-based discovery platform
Gilead	Scholar Rock	Dec-2018	Discovery	1,530	80	1,450	Fibrotic diseases	<ul style="list-style-type: none"> Exclusive WW right to license three products from Scholar Rock's transforming growth factor beta activation programs
Johnson & Johnson	Yuhan	Nov-2018	Phase II	1,255	50	1,205	Oncology	<ul style="list-style-type: none"> Exclusive WW ex-Korea rights to Lazertinib, a therapy for non-small cell lung cancer
AbbVie	Lupin	Dec-2018	Preclinical	977	30	947	Oncology	<ul style="list-style-type: none"> Exclusive rights to Lupin's MALT1 inhibitor programs for hematological cancers
Xynomic Pharma	Boehringer Ingelheim	Dec-2018	Phase I	800	-	-	Oncology	<ul style="list-style-type: none"> Exclusive rights to BI 860585, a mTORC1/2 inhibitor for solid tumors

SOURCE: Locust Walk analytics, BioSciDB, Global Data

2018 set records for volume, but total value did not surpass records in 2014 and 2015

WW Biopharma Therapeutic M&A Deals (>\$100M)



SOURCE: Locust Walk analytics, Pitchbook; *Locust Walk has altered methodology beginning Q3 2017, previous reports' numbers may not reflect this. Data includes Takeda/Shire

Although Q4 M&A deal volume and value decreased from Q3, there were some notable transactions



SOURCE: Locust Walk analysis

In Q4, the FDA approved 18 new therapies, for a total of 59 new therapies approved in 2018

Select Approvals

<p>Seysara To treat severe acne vulgaris Allergan/Paratek 10/1</p>	<p>Talzenna To treat breast cancer Pfizer 10/16</p>	<p>Daurismo To treat acute myeloid leukemia (AML) Pfizer 11/21</p>
<p>Nuzyra To treat community acquired bacterial pneumonia (CABP) Paratek 10/3</p>	<p>Xofluza To treat the flu Genentech 10/24</p>	<p>Vittrakvi To treat cancers with specific genetic biomarkers Loxo Oncology 11/26</p>
<p>Tegsedi To treat hereditary transthyretin-mediated (hATTR) amyloidosis Akcea Therapeutics 10/5</p>	<p>Lorbrena To treat non-small cell lung cancer (NSCLC) Pfizer 11/2</p>	<p>Firdapse To treat Lambert-Eaton myasthenic syndrome (LEMS) Catalyst 11/28</p>
	<p>Gamifant To treat hemophagocytic lymphohistiocytosis (HLH) Sobi 11/20</p>	<p>Ultomiris To treat paroxysmal nocturnal hemoglobinuria (PNH) Alexion Pharmaceuticals 12/21</p>

SOURCE: Locust Walk analytics, Fierce Biotech, Fierce Pharma, FDA

Contact Info

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For more information, visit us at www.locustwalk.com

BIOPHARMA EUROPE

Europe Biopharma Financing - Private

Red-hot EU VC investment climate in 2018

- EU VC investment has been fast-paced and has risen quickly in aggregate value
- Robust series A investment in 2016 and 2017 has led to a greater than double increase in series B investments in 2018: 25 series B rounds totaling \$781M in 2018 v. 15 rounds totaling \$376 in 2017

Given the uncertainty of the European public markets, Locust Walk expects companies to see the continued strength in EU VC and other private investment for 2019

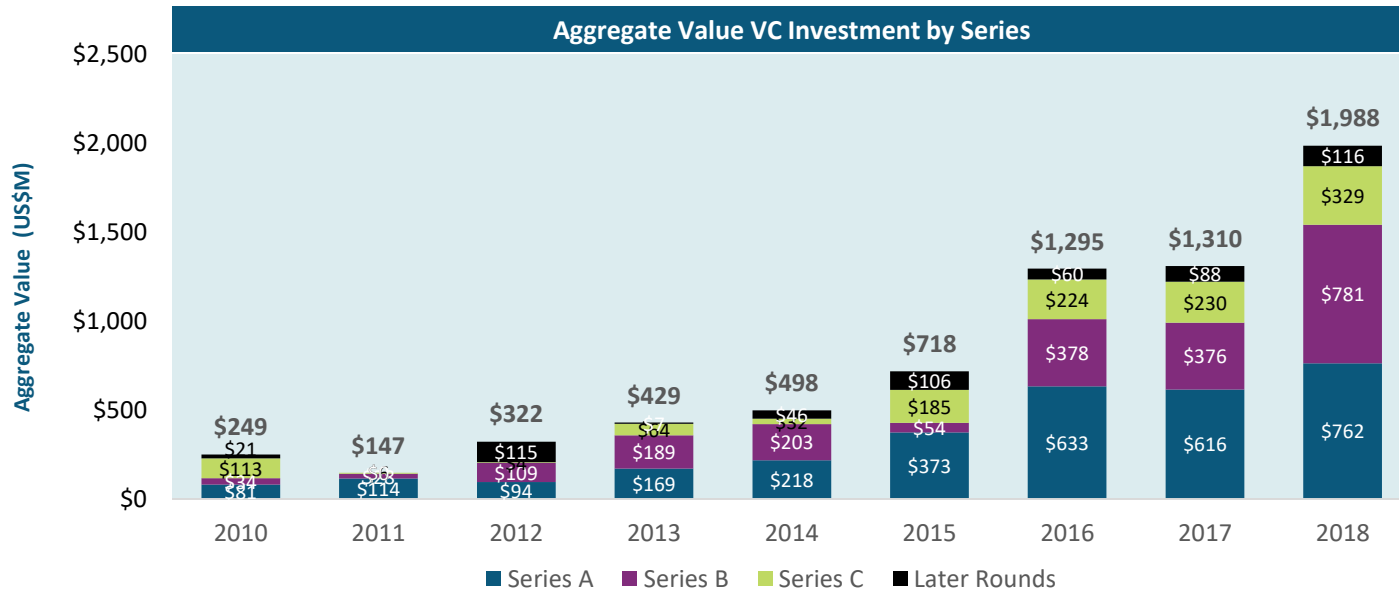
- Private EU companies to leverage existing investors for another private or cross-over round
- As assets in gene therapy, immuno-oncology, orphan disorders enter the clinic, we expect companies with innovative programs to be able to complete larger financings with private investors in 2019
- Companies expected to deliver following big financings in 2018, some companies have big data read outs

Europe Biopharma Financing - Public

Strong EU biotech companies find public market success on US stock exchange

- Promising European companies continued successful fundraising on US exchanges (Nasdaq)
 - British gene therapy company Orchard Therapeutics raised \$200M in Q4 2018 (IPO)
 - Argenx raised \$300M in an offering to qualified investors in the US and Europe (secondary offering)
 - German mAb company Morphosys raised \$239M (secondary offering)
- European IPOs listed on EU stock exchanges experienced a slow down after a busy 1H that saw 5 biopharma IPOs and 2 secondary public offerings; raising \$907M
- 1H 2018 was headlined by a \$466M raise by Dermapharm, a German generic company, in Q1 and \$163M and \$155M raises by Polyphor and Cellectis respectively in Q2
 - Only 5 IPOs in 2H 2018 totaling \$80M: Two EU biopharma IPOs close in Q4 2018 – raising a total ~30M
- Slowdown potentially linked to geopolitical changes and trade tensions
 - Brexit, esp. if hard, will affect companies seeking to go public in Europe or raise 2ndary financings
- Selected EU companies to list or raise in the US, potentially moving their HQ to the East Coast
- With uncertain public markets In Europe and UK, companies need to focus on deal making

2018 is a record year for EU private financing



Deals (#)	2010	2011	2012	2013	2014	2015	2016	2017	2018
A	16	19	19	21	26	33	37	38	32
B	4	4	11	14	10	5	14	15	25
C	3	1	1	3	1	7	7	6	5
D & Later	2	0	3	1	1	1	1	2	2
Total	25	24	34	39	38	46	59	61	62

SOURCE: Locust Walk Analysis, Pitchbook Methodology: All US series A, B, C, D, and later investments; Healthcare > Pharmaceuticals and Biotechnology Industry only; EU HQ only

The fourth quarter saw 2 IPOs from EU biopharma

EU Q4 IPOs										
Offering Type	Biopharma Issuer	Ticker	Key Therapeutic Area	Lead Phase	Offer Date	Price Range	Offering Price	Total Raise	Price Change to 1/1/19	Market Cap 1/1/19
IPO	AlzeCure Pharma Huddinge, Sweden	ALZCUR STO	CNS	Phase I	28/11/18	N/A	\$1.54	\$22M	\$0.95	\$36M
IPO	Pure Biologics Wroclaw, Poland	PUR WAR	Oncology	Preclinical	11/12/18	N/A	\$5.88	\$0.75M	\$5.21	\$0.66M



Summary

- AlzeCure is focused on developing disease modifying and symptomatic first in class treatments for Alzheimer's disease and other conditions characterized by cognitive dysfunction
- Proprietary technology platforms enable the rapid and efficient generation of recombinant proteins and antibodies

Key Program(s)

- NeuroRestore: Development of druglike compounds that stimulate neurotrophic signaling and the function of neurons resulting in improved memory
- Alzstatin: Gamma-secretase mediated reduction of Alzheimer-related A β 42 to delay or prevent the onset of disease
- Multi Body: Bispecific recombinant antibody inducing targeted activation of T lymphocytes for cancer immunotherapy

SOURCE: Locust Walk analysis, EDGAR Company Filings, Yahoo Finance, Pitchbook, Methodology: EU IPOs in 2018. Healthcare > Pharmaceuticals and Biotechnology (Primary Industry only), EU HQ only; Ad hoc addition of companies filing secondary offerings on US exchanges (i.e. ADS)

Europe Biopharma Transactions (1/2)

Robust year over year growth in EU M&A

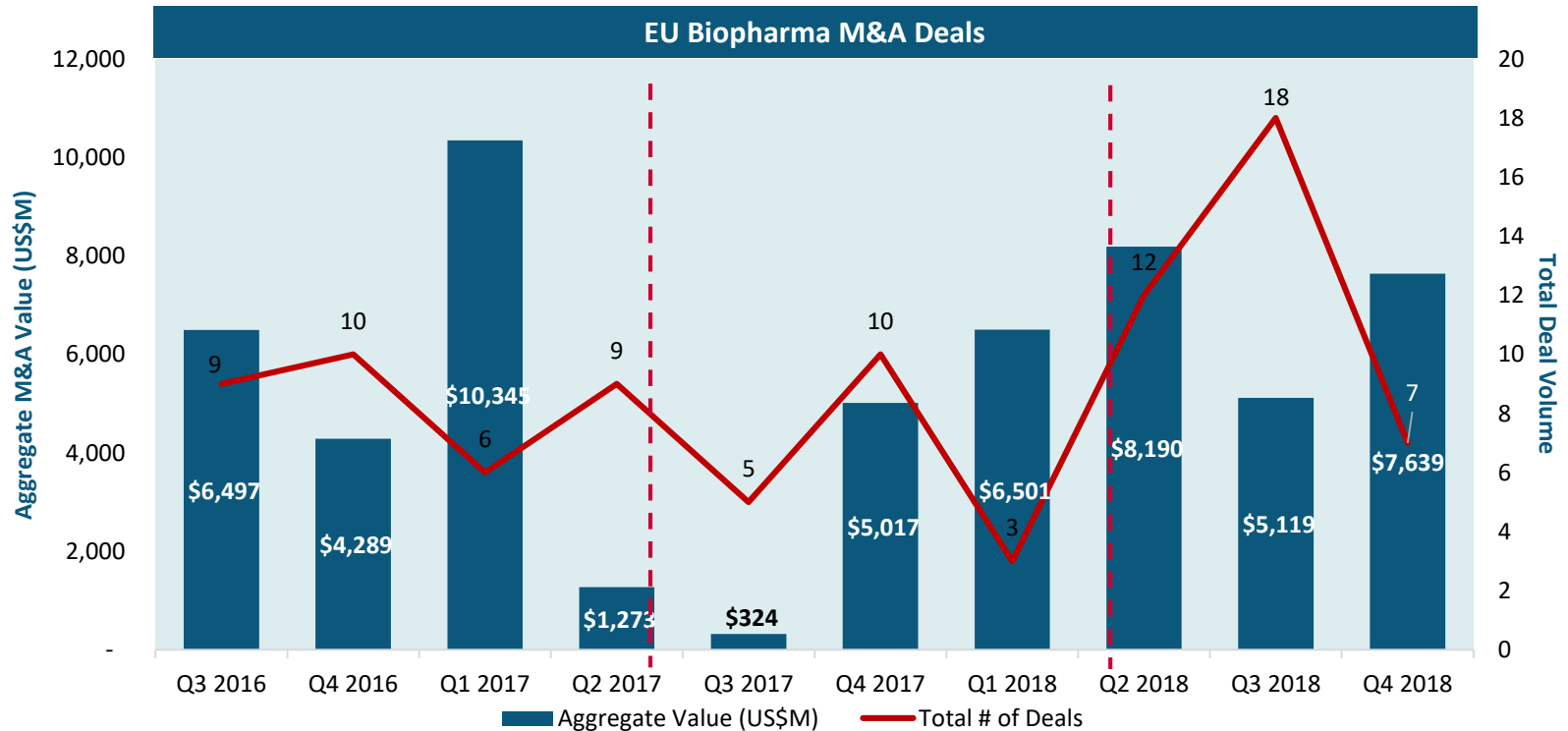
- The EU saw the largest M&A volume in more than a year: a greater number of blockbuster deals (>\$1B) resulted in a higher average deal value in 2018 as opposed to 2017 (~145M higher)
 - Notably, GSK's acquisition of oncology company Tesaro for \$5.1B,
 - Sanofi to acquire Ablynx for \$4.8B (a bet that began paying immediate dividends with EMA approval of Cablivi in April), and
 - Takeda reinforcing its commitment to inflammatory bowel disease by acquiring TiGenix for \$608M
- Business sell-offs contributed to growth in M&A:
 - Merck sold its consumer health unit to Proctor and Gamble for \$4.2B and
 - Servier acquired Shire's oncology business unit for \$2.4B
 - AstraZeneca to divest US rights for Synagis to SOBI for \$1.5B upfront plus future payments
- Locust Walk expects to see this trend continue as overall investment and innovation is on the rise and pharma companies will seek to streamline their portfolio to focus investments in core therapeutic areas and maximize the value of non-core assets.

Europe Biopharma Transactions (2/2)

Locust Walk expects an upswing in 2019 licensing given the uncertainty in public markets

- After a slow start to 2018 licensing, oncology deals led the back half of 2018 in total value and volume
 - Janssen licenses anti-CD70 Cusatuzumab from Argenx for the treatment of AML (\$265 upfront payment up to \$1.6B in milestones)
 - Allogene acquires license with Cellectis from Pfizer to develop 15 targets for up to \$185M each
- Dermatology and CNS contribute to majority of remaining licensing activity
 - Novartis acquired the development and commercialization rights to MOR10 from Morphosys for the treatment of atopic dermatitis (\$1B)
 - Eli Lilly to continue their investment in Alzheimer's Disease by acquiring tau aggregation inhibitor from AC Immune (\$1.7B)
- Locust Walk expects pharma companies to increasingly look to the EU to acquire interesting platforms or therapeutics as the science is strong and valuations are attractive for buyers
- Gene therapy deals to pick up, less activity in I-O combination therapies, cancer vaccine programs on the rise
- Increased deal activity expected in other therapeutic areas, esp. orphan or rare disorders

GSK acquisition of Tesaro represents bulk of Q4 2018 M&A activity



SOURCE: GlobalData, Pitchbook; Methodology: Target Company HQ Located in EU, Pharmaceuticals and Biotechnology; Deals without size disclosed are excluded; Deal date reflects the announced date. Select major global deals are excluded from this dataset, and displayed in the US biopharma section of the report.

Q4 rebounds from a lackluster Q3 for EU M&A biopharma transactions

Locust Walk expects robust growth to continue given continued innovation in EU biotech

December 21, 2018



Endocyte acquired by Novartis AG for \$2.1B

Acquisition of Endocyte further strengthens Novartis' expertise in radiopharmaceuticals, adding ¹⁷⁷Lu-PSMA-617, a first-in-class radioligand therapy in Phase III, to its pipeline. Endocyte uses drug conjugation technology to develop targeted therapies for metastatic castration-resistant prostate cancer.

December 18, 2018



Croda to acquire Brenntag Biosector for \$81M

Brenntag Biosector, is a specialist in the manufacture and supply of adjuvants serving the human and veterinary vaccine market. Biosector unique product portfolio centers around innovative alumni and saponin-based adjuvants.

December 3, 2018



GSK to acquire TESARO for \$5.1B

Tesaro is a commercial-stage oncology company that has marketed Zejula, an oral PARP inhibitor currently approved for ovarian cancer. Indication expansion trials for Zejula are underway. Tesaro has several oncology assets in its pipeline including antibodies direct against PD-1, TIM-3, and LAG-3.

October 1, 2018



Sangamo acquires TxCell for \$84M

TxCell pioneer CAR-Treg programs will be integrated with Sangamo's zinc finger nuclease technology to develop cutting edge genetic editing technologies for the treatment of autoimmune, inflammatory, and transplantation related disorders. In 2019, Sangamo is expected to submit a CTA for TxCell's first investigational product, accelerating Sangamo's entry into the clinic.

SOURCE: Locust Walk analysis

Select EU licensing deals in Q4 2018

The oncology space in the EU is red-hot with several exciting high value collaborations. Cilag's global collaboration and license agreement with argenx led the quarter (\$1.6B total deal size)

Licensee	Licensor	Announced Date	Therapeutic Area	Upfront (\$M)	Total Deal Size (\$M)	Comments
Boehringer Ingelheim	Xynomic Pharmaceuticals	20-Dec-2018	Oncology	N/A	800	BI 860585 is a phase II ready mTORC1/2 inhibitor – adding to Xynomic's mid-stage pipeline.
Molecular Partners	Amgen	18-Dec-2018	Oncology	50	547	Amgen obtains global development and commercial rights for MP0210 a immune modulator of 4-1BB
AC Immune	Eli Lilly	12-Dec-2018	CNS	130	1,716	R&D collaboration agreement to develop tau aggregation inhibitor for Alzheimer's disease
Wuxi Biologics	Oxford BioTherapeutics	11-Dec-2018	Oncology	N/A	450	Oxford licensed five bispecific antibodies - taking advantage of WuXiBody manufacturing platform
Argenx	Janssen / Johnson & Johnson	03-Dec-2018	Oncology	300	1,600	Worldwide license agreement for cusatuzumab, an investigation antibody targeting CD70 checkpoint inhibitor currently in phase I/II
Idorsia Pharmaceutical	Santhera Pharmaceuticals	20-Nov-2018	Musculoskeletal	20	435	Santhera acquires exclusive sub-license of first-in-class dissociative steroid vamorolone currently in a pivotal phase 2b
iNtRON Biotechnology	Roivant Sciences	19-Nov-2018	Infectious Disease	N/A	667	Global licensing agreement for SAL200, a phase II ready novel investigational biologic for antibiotic-resistant staphylococci
Kolon Life Science	Mundipharma International	19-Nov-2018	Orthopedic	27	594	Exclusive rights for the development, marketing and distribution of the cell-mediated gene therapy Invossa
AstraZeneca	Swedish Orphan Biovitrum	13-Nov-2018	Infectious Disease	1,500	1,970	To refocus on priority drugs, AstraZeneca sold US rights to a treatment of infant lung infections
Enterome Bioscience	Takeda Pharmaceutical	30-Oct-2018	Inflammation	50	690	Takeda expands their microbiome focused assets in a co-development agreement
Zymeworks	LEO Pharma	23-Oct-2018	Dermatology	5	480	Licensing and research collaboration to develop and commercialize two bispecific candidates in dermatology infections

SOURCE: Locust Walk analysis; Global Data. Methodology: EU licensing transactions >\$90M

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BIOPHARMA ASIA

Japan BioPharma Transactions

Volatility of shares of the top 40 Japanese biotech companies in 2018 was much greater than 2017 with overall weak performance since Q2, seeing a downward trend, ending -19% YoY in 2018

- PeptiDream saw a sharp decline in Q2 after its announcement of the departure of the company founder; however, they recovered in the following quarters but still struggling to recover levels before Q2 levels
- SanBio saw a steep hike in valuation in November driven by the top line result of its Phase 2 studies for SB623 cell therapy for traumatic brain injury ending 2018 with a market cap exceeding \$3.7B, second highest in the group following PeptiDream of \$4.7B
- Takara Bio has also enjoyed an exceptionally strong year primarily driven by its licensing activities with Otsuka in April, Dong-A ST (South Korea) in August, and Daiichi Sankyo in September albeit other peers suffering from constant declines in share prices

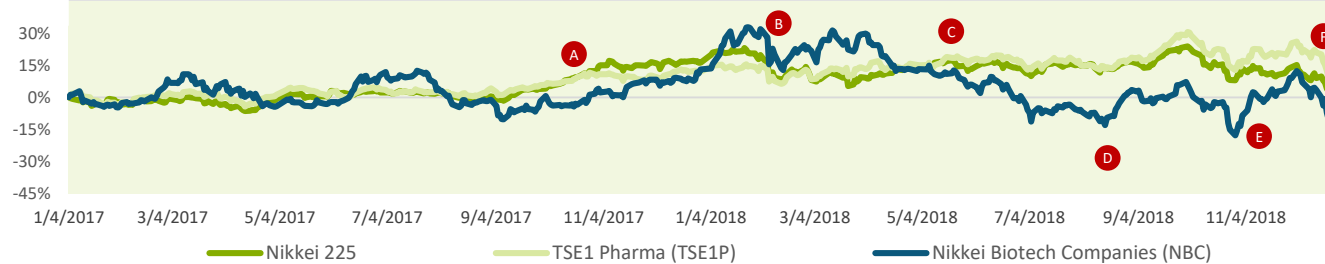
Share prices of 39 major pharmaceutical companies listed on the 1st Section of Tokyo Stock Exchange (TSE1) outperformed the Nikkei 225 in Q4, however market performed -6% since Jan 2018

The volume of Japan licensing deals with announced size of >\$10M in 2018 hit record highs since 2008; Takeda's acquisition of Shire was the biggest deal across all M&A deal history by a Japanese company

Biotech shares have suffered from the worldwide stock price plunges toward the end of 2018

Q4 2018 and Historical Performance of key Market Indices

	Q1 2017	Q2 2017	Q3 2017	Q4 2017	Q1 2018	Q2 2018	Q3 2018	Q4 2018
ΔNikkei 225(%)	(1.1%)	5.9%	1.6%	11.8%	(5.8%)	4.0%	8.1%	(17.0%)
ΔTSE1P (%)	(1.5%)	4.3%	1.9%	6.0%	1.8%	2.5%	10.7%	(16.8%)
ΔNBTC (%)	(12.2%)	4.1%	(11.2%)	15.3%	14.3%	(22.2%)	5.4%	(13.9%)



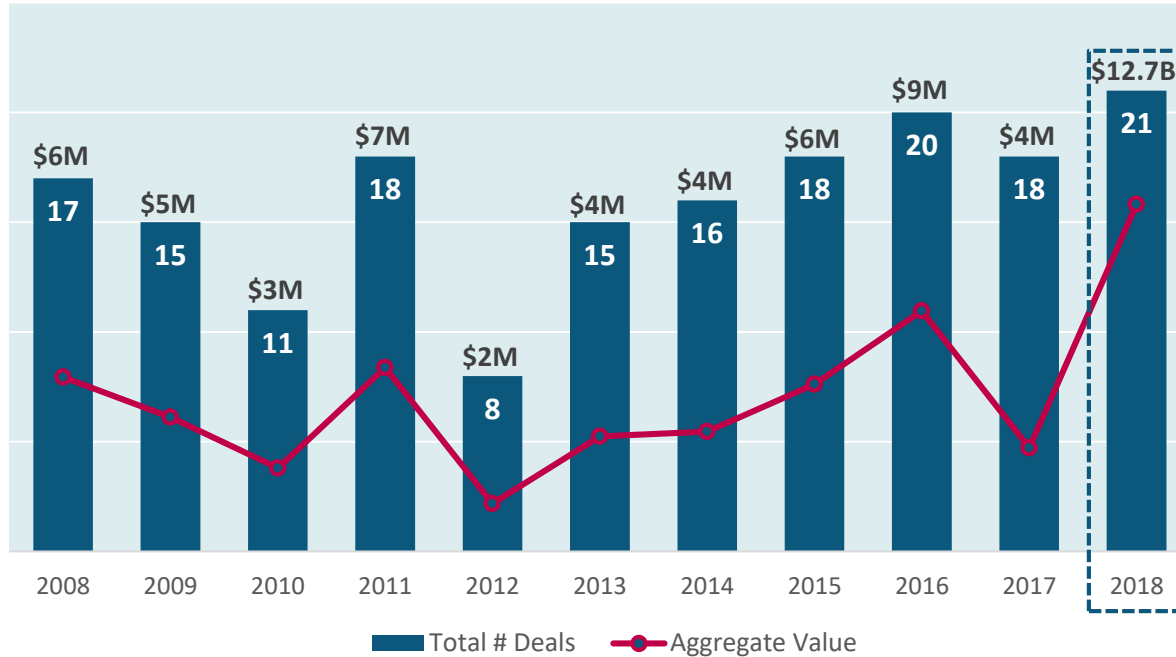
Key Event	
A	Nikkei 225 set a 21-year high in Oct. after its longest winning streak; the upward trend has been reflected in the biotech companies
B	NBC fell in line with Nikkei 225's radical fall after the US market suffering from heavy losses in February
C	May 8, 2018: Takeda Pharmaceutical agreed to buy Shire for \$62 billion, which made Takeda a global pharmaceutical leader
D	September 9, 2018: Delta-Fly Pharma announced its IPO to MOTHERS in October; it was the only biopharma IPO in Japan in 2018
E	SanBio led the sharp recovery of NBC since the worldwide decline of stock prices by its successful global Ph2 data readout for SB623
F	December 28, 2018: TSE1P and NBC close -5.78% and -19.50%, respectively, since the beginning of 2018

SOURCE: Locust Walk Analytics; Nikkei BioTech Online; Yahoo! Japan Finance

* MOTHERS (Market of the high-growth and emerging stocks): The stock market at the Tokyo Stock Exchange for emerging businesses, including Sosei Group, Green Peptide, and Solasia

2018 Japan deal activity has been brisk, ending up with >20 deals having aggregate value of >\$12B

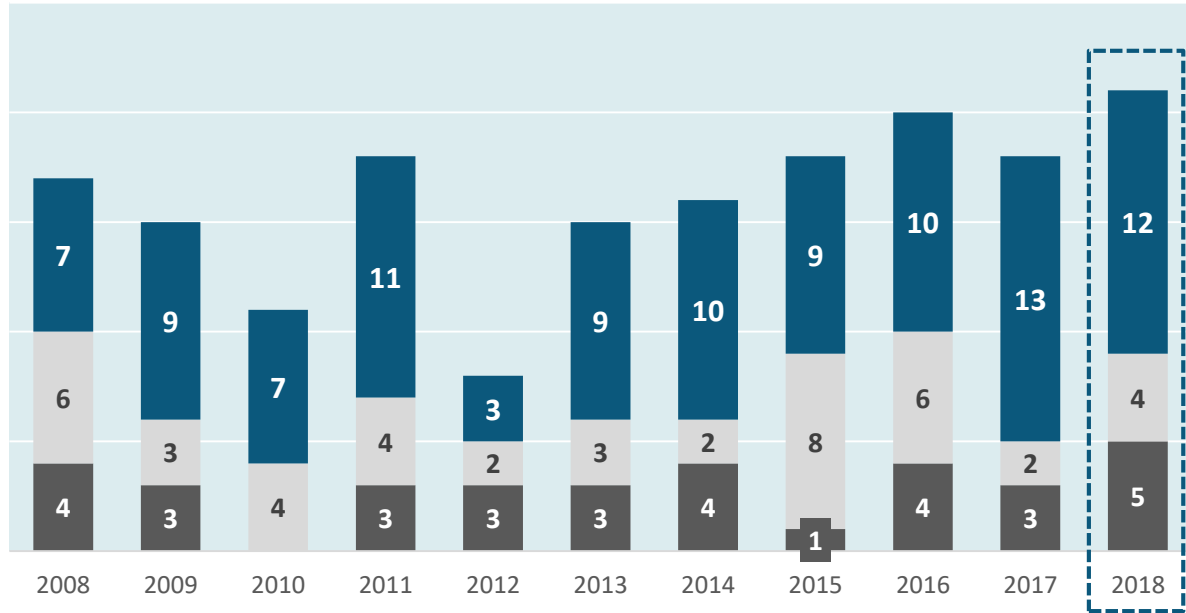
Biopharma deals >\$10M (announced deal size basis)



SOURCE: Locust Walk Analytics, BioSciDB, GlobalData, Pharma Japan Web

>55% of deals having >\$10M in value has involved late stage assets

Biopharma deals >\$10M (announced deal size basis)



■ Early Stage (Discovery + Lead) ■ Mid Stage (Preclinical + Phase 1) ■ Late Stage (Phase 2, Phase 3, NDA, Approved)

SOURCE: Locust Walk Analytics, BioSciDB, GlobalData, Pharma Japan Web

Six sizable in-licensing deals with >\$10M; out-licensing and M&A remained smaller for Q4

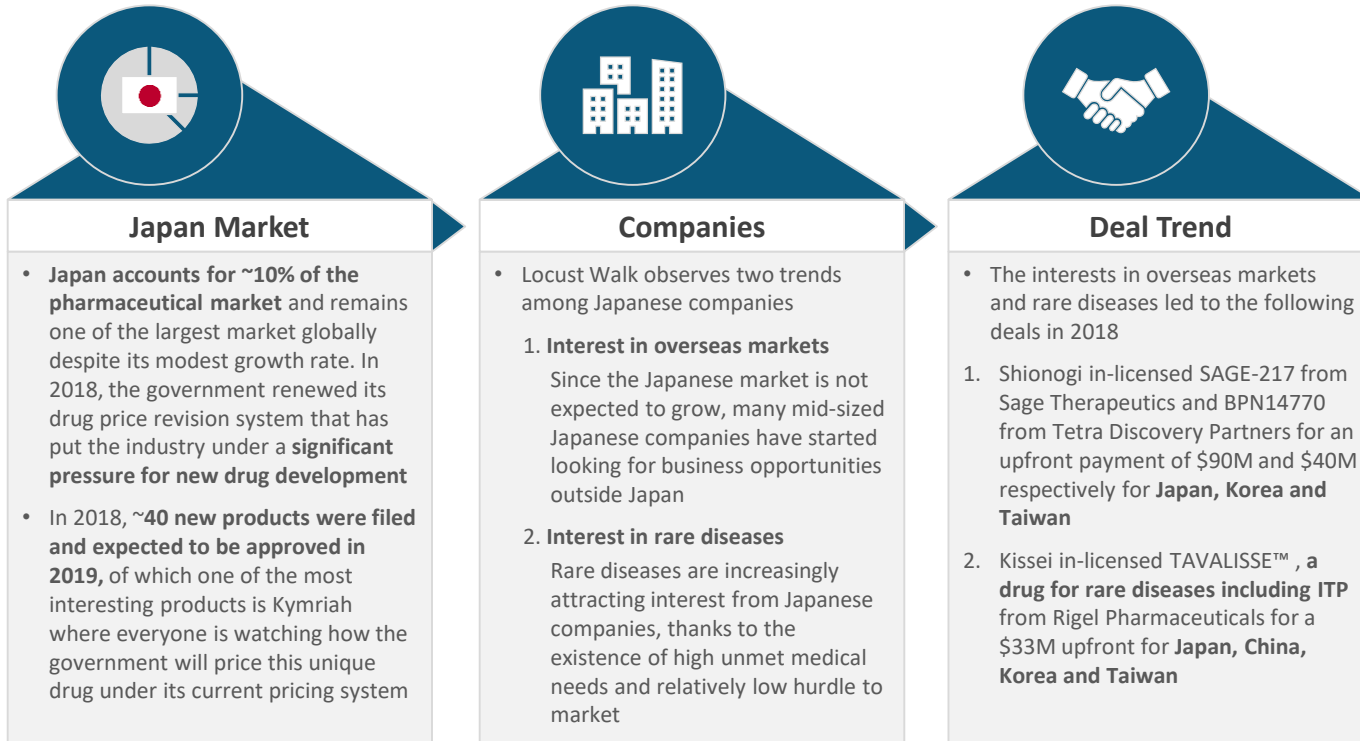
Licensee	Licensor	Date	Stage	Deal Size (\$M)	Subject
Tetra Discovery Partners	Shionogi	12/2018	Phase II	160	Co-development and commercialization of BPN14770 for CNS diseases
Kolon Life Science	Mundipharma	11/2018	Phase III	600	License agreement for INVOSSA®, a cell-mediated gene therapy for osteoarthritis in Japan
MEI	Kyowa Hakko Kirin	11/2018	Phase II	88	License agreement for ME-401 for the treatment of patients with B-cell malignancies
Rigel Pharmaceuticals	Kissei	10/2018	Phase III	180	License agreement for TAVALISSE™ for thrombocytopenia and other indications in Asian countries
Enterome Bioscience	Takeda	10/2018	Phase I	640	Global licensing, co-development and co-promotion agreement for EB8018 for Crohn's disease
Molecular Templates	Takeda Millennium	10/2018	Preclinical	663	Collaboration agreement for oncology drug discovery programs

Astellas exercised the option for the buyout of the US immuno-oncology startup

Seller	Buyer	Date	Deal Size (\$M)	Subject
Potenza	Astellas	11/2018	240	Acquisition of a US biotech developing novel cancer immunotherapies

NOTE: Japan pharmas are indicated in bold letters

Japanese companies remain hungry to in-license, with increasing interest from other Asian markets



Japan/Asian partnering is recommended to consider as a source of non-dilutive funding

China BioPharma Financing and Transactions

2018 was a weak year for Chinese public pharmaceutical companies partially due to US-China trade war and the enormous drug price cuts in recent tenders

- Top 20 China mainland listed pharmas have seen their stock prices drop 23.7% on average while the SSE composite Index closed -25.5%* YoY
- Leading pharmas, such as Hengrui and Fosun, have also seen its stock price go down by 23.2% and 46.8%, respectively

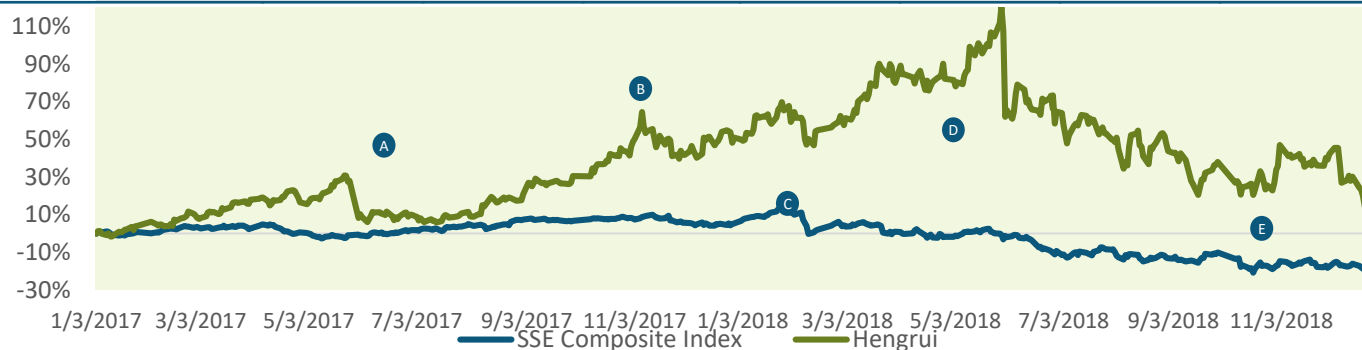
6 Biopharma companies listed in Hong Kong and raised \$3,195M in total

- BeiGene, which is listed in NASDAQ under the ticker BGNE raised \$903M after its secondary listing in Hongkong
- Wuxi AppTec also successfully raised \$967M following its Shanghai debut in Mar 2018 where it raised \$910M

In-licensing deal volume increased to 63 (+75% YoY 2017) mainly led by young biopharma companies, continuously focusing in the oncology space

“US-China trade war” has been a drag for Chinese equities leading to mediocre performance

2018 and Historical Performance of SSE Composite Index and Hengrui								
	1Q 2017	2Q 2017	3Q 2017	4Q 2017	1Q 2018	2Q 2018	3Q 2018	4Q 2018
ΔSSE Composite Index %	2.7%	1.8%	6.8%	5.5%	1.1%	(9.2%)	(10.0%)	(20.5%)
ΔHengrui %	18.0%	10.0%	30.3%	50.0%	89.2%	64.7%	38.0%	14.7%

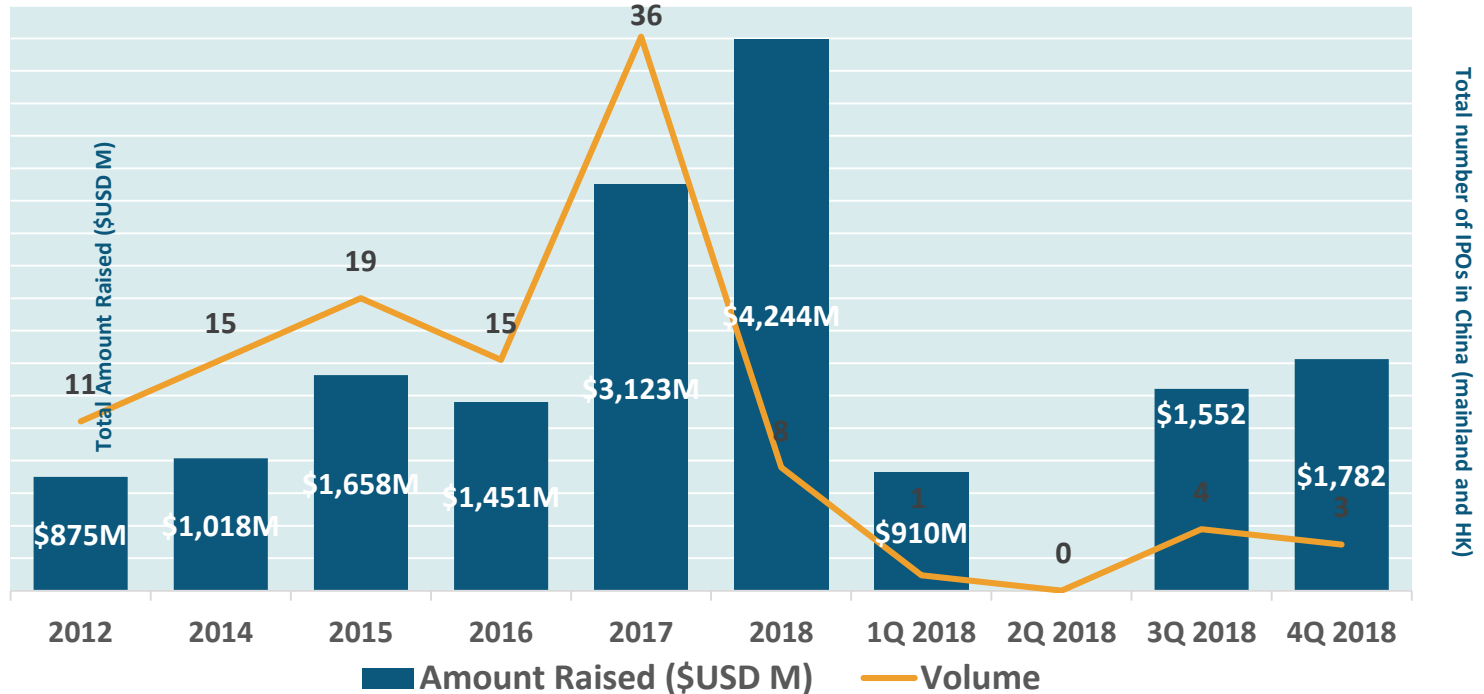


Key Event
A Following the release of 2016 annual and Q1 report in Mar and Apr, the price has since appreciated to 60.2CNY (+10.5% vs. Jan 2017)
B Stock price of Pharmaceutical companies have seen their price soar including Hengrui
C SSE composite index has seen its price drop due to the poor performance of US stock market
D Listed 845 million of common stock
E SSE composite index closed at 2,493.9 (-25.5% YoY 2018)

SOURCE: Locust Walk Analytics, Yahoo Finance

The China capital markets raised \$4.2B in 2018 of which \$3.2B came from Hong Kong

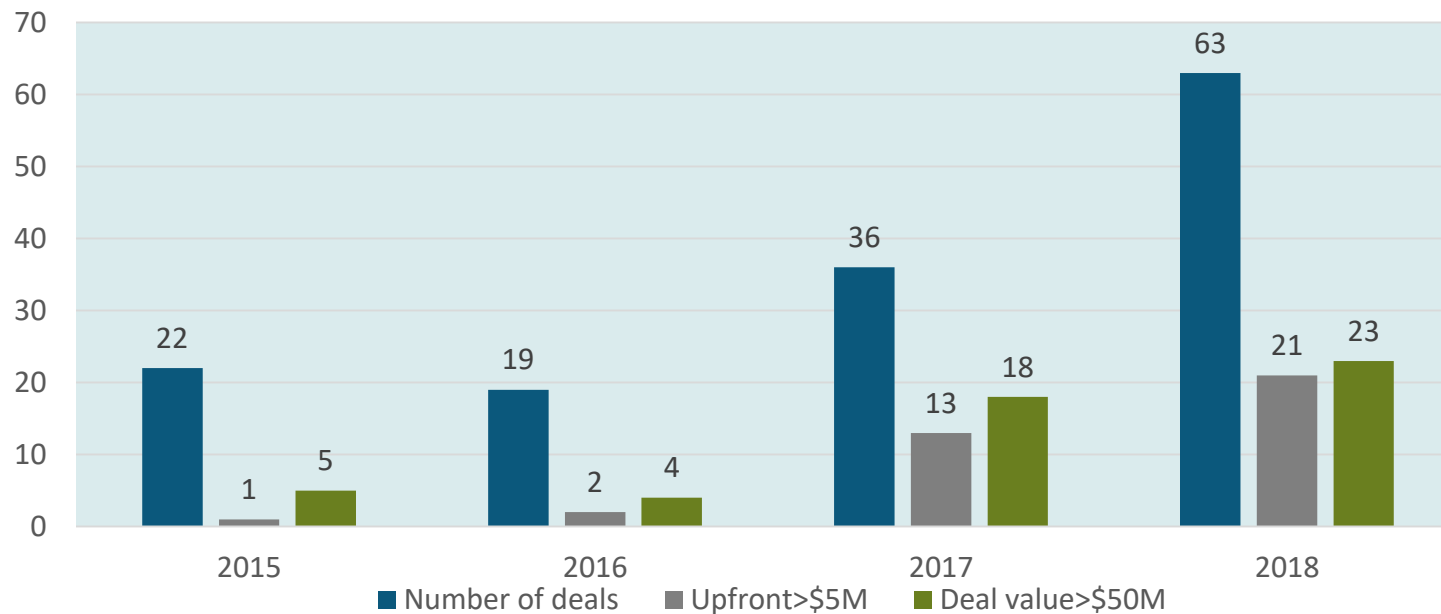
Number of Biopharma IPOs and Aggregate Total Raised By Quarter



SOURCE: Locust Walk Analytics; Eastmoney, ChinaBio® Today

The number of in-licensing deals significantly increased as well as the upfront payment & total deal value

Trend of in-licensing deals in China (number of deals)



SOURCE: Locust Walk Analytics, ChinaBio® Today, Globaldata

Deal volume is rising driven by available capital, overseas returnees and improved regulatory environment

- **In-licensing deal volume has significantly increased with substantial front-end economics**
 - 21 deals with upfront payment >\$5M
 - 23 deals with total deal size >\$50M
 - Beigene acquired Asia (ex-Japan) rights of 2 oncology candidates from Zymeworks with a total of \$430M which includes a \$40M upfront, marking the largest in-licensing deal in China
 - Innovent paid a \$40M upfront for Greater China rights for 3 oncology assets of Incyte
- **Zhejiang Bossan and I-Mab out-licensed ex-China rights of their candidates to maximize the product commercial potential**
 - Zhengjiang Bossan granted CBT Pharma the global rights (ex-Greater China) of ES-702, a novel EGFR inhibitor, deal value is not disclosed
 - ABL Bio acquired exclusive global rights (ex-Greater China) to two novel IO mAb sequences from I-Mab, ABL Bio will pay \$2.5M upfront and up to \$100M milestones as well as royalties
- **Some M&A activity was seen as well**
 - Huadong Medicine acquiring Sinclair Pharma for \$220M
 - Shanghai's biopharma investment firm SARI acquired an Italian oncology biopharma NMS Group for \$359M

SOURCE: Locust Walk Analytics, ChinaBio® Today, Globaldata

Key China in-licensing deals in 2018 (1/2)

Licensor	Licensee	Area/Indication	Date	Stage	Upfront (\$M)	Total deal (\$M)
Nicox	Ocumension Therapeutics	Ophthalmology	12/2018	Ph2	3.4	41.5
Incyte	Innovent	Oncology	12/2018	Multiple assets transaction	40.0	391.5
VBI Vaccines	Brii Biosciences	Hepatitis B Vaccine	12/2018	Ph3	4.0	121.5
Zymeworks	BeiGene	Oncology	11/2018	Multiple assets transaction	40.0	430.0
MacroGenics	Zai Lab	Oncology	11/2018	Multiple assets transaction	25.0	165.0
MorphoSys	I-Mab	Oncology (Multiple myeloma)	11/2018	Phase 1/2a	20.0	120.0
Medical Developments	Daiichi Sankyo	Pain (Non-Opioid Analgesic)	10/2018	Approved	15.0	32.5
DiaMedica	Jinzhou Ahon (Fosun)	Stroke	09/2018	Phase 2	5.0	32.5
Verastem	CSPC Pharma	Hematology oncology	09/2018	Approved	15.0	45.0
Novocure	Zai Lab	Oncology	09/2018	Approved	15.0	15.0
Synergy Pharma	Luoxin	GI	08/2018	Approved	12.0	68.0
Mesoblast	Tasly	CV	07/2018	Phase 2/3	40.0	65.0
Agio	CStone	Oncology	06/2018	Pre-registration	12.0	424.0

SOURCE: Locust Walk Analytics, ChinaBio* Today, Globaldata

Key China in-licensing deals in 2018 (2/2)

Licensor	Licensee	Area/Indication	Date	Stage	Upfront (\$M)	Total deal (\$M)
Pacira Pharma	Nuance Biotech	Pain	06/2018	Approved	3.0	58.0
CrystalGenomics	Aptose	Oncology	06/2018	Pre-clinical	3.0	125.0
Blueprint	CStone	Oncology	06/2018	Multiple assets transaction	40.0	386.0
Karyopharm	Antengene	Oncology, anti-viral	05/2018	Multiple assets transaction	12.0	162.0
Adocia	Tonghua Dongbao	Type 2 Diabetes	04/2018	Phase 1b	40.0	90.0
Adocia	Tonghua Dongbao	Type 1 Diabetes	04/2018	PK study	10.0	45.0
Entasis Therapeutics	Zai Lab	Antibiotics	04/2018	Phase 2	5.0	114.0
Tocagen	Apollo Bio	Oncology	04/2018	Phase 2/3	16.0	127.0
Nabriva	Roivant	Antibiotics	03/2018	Ph3	5.0	95.0
Tetraphase Pharma	Everest Medicines	Antibiotics	02/2018	NDA	7.0	43.5
Mologen	Oncologie	Oncology	02/2018	Ph3	6.2	126.2
Puma Biotech	Canbridge	Oncology	02/2018	Approved	30.0	70.0
Mirati Therapeutics	BeiGene	Oncology	01/2018	Ph2	10.0	133.0

SOURCE: Locust Walk Analytics, ChinaBio* Today, Globaldata

2019 China market in perspective



Market and regulatory

- **China is now the 2nd largest healthcare market in the world** and expected to grow further due to continued economic growth and an aging society
- **In 2018, NMPA approved 48 new drugs, including 38 imported drugs and 10 domestic companies developed drugs;** a CKD new drug, Roxadustat, obtained China-first-approval by AstraZeneca China
- **As NMPA is aiming to be more aligned with global regulatory standards,** such as data exclusivity, there remains uncertainty as to whether it will be enacted



R&D focus

- We observe two trends among Chinese companies
 - 1. Mainly develop me-too or me-better assets**

Due to the relatively limited new drug R&D experiences and risk control, first-in-class assets are rarely seen in China
 - 2. New drug development concentrated in oncology**

Favorable regulations for development fueled interest in oncology. However, specialty therapeutic areas such as neuroscience, dermatology and ophthalmology are still untapped



Potential Challenges

- With a premature pricing system and the Chinese government trying to cut drug prices, **as more and more me-too or me-better drugs are approved, a price war might be inevitable as the government has the power to control the National Reimbursement Drug List**
- As seen by the volatility of the biotech stocks newly listed on the HongKong Exchange, it may take some time for the market to adjust to these new market entrants with high expectations
- Despite improvement in IP protection actual implementation of these reforms are still in the working

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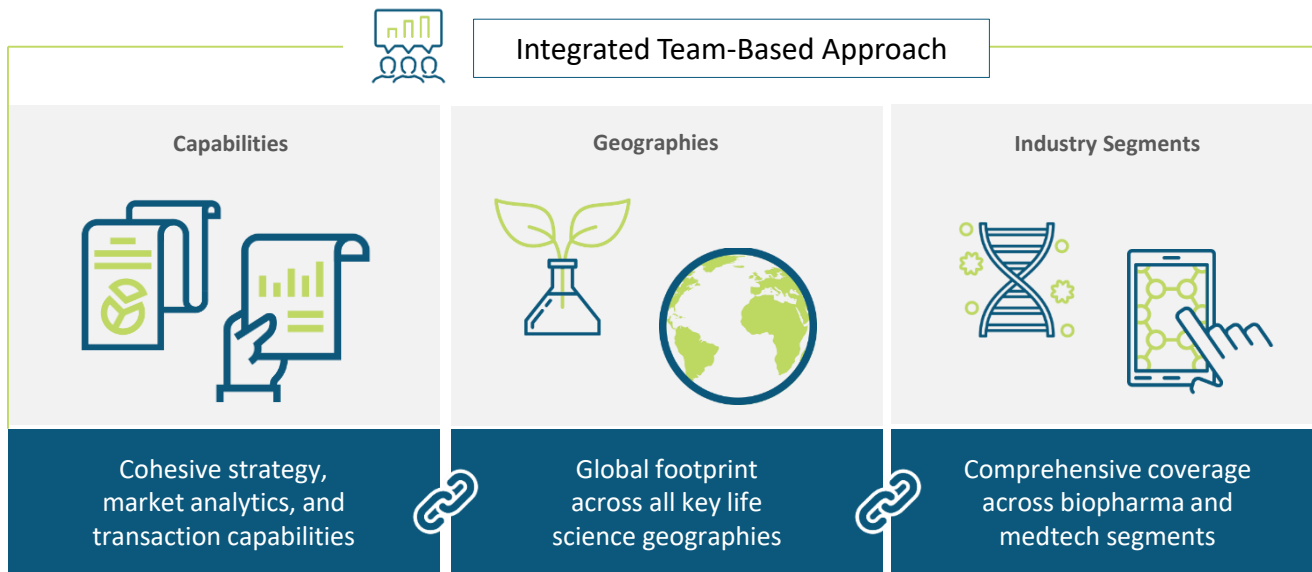
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ABOUT LOCUST WALK

Locust Walk is a global life science transaction firm.

Our integrated team-based approach across capabilities, geographies, and industry segments delivers the right products, the right partners, and the most attractive sources of capital to get the right deals done for biopharma and medtech companies.



Locust Walk is the only firm to integrate strategy, market analytics, and transaction capabilities from both biopharma and medtech perspectives on a global scale

Capabilities

Cohesive strategy,
market analytics, and
transaction capabilities

- One integrated team focused on your entire deal process.
- Track record of addressing key strategic questions for companies at the corporate, portfolio, and asset levels, so we have the experience to execute most any deal from licensing to M&A to financing.
- Strategy capabilities generate holistic alternatives, actionable commercial strategies, and a powerful value prop.
- Our market analytics capabilities lay the foundation to evidence-based strategies that support groundbreaking deals and partnerships.
- Our transaction process—beginning with an upfront transactability diagnostic and valuation— ensures that you realize maximum deal value in a timely manner, outweighing the opportunity costs of alternative transactions.

Geographies

Global footprint
across all key
life science geographies

- On-the-ground presence in all major life science markets across the United States, Europe, and Asia.
- Offices are staffed with local teams, who also have experience working around the globe.
- Experience ensures that we maintain relationships with local companies and investors, can navigate cultural and language differences, and have a feel for geography-specific trends impacting the deal landscape.
- Maintaining a global presence enables us to tap a combination of deal sources regardless of where they reside, so that your deal isn't limited by geographical borders.

Industry Segments

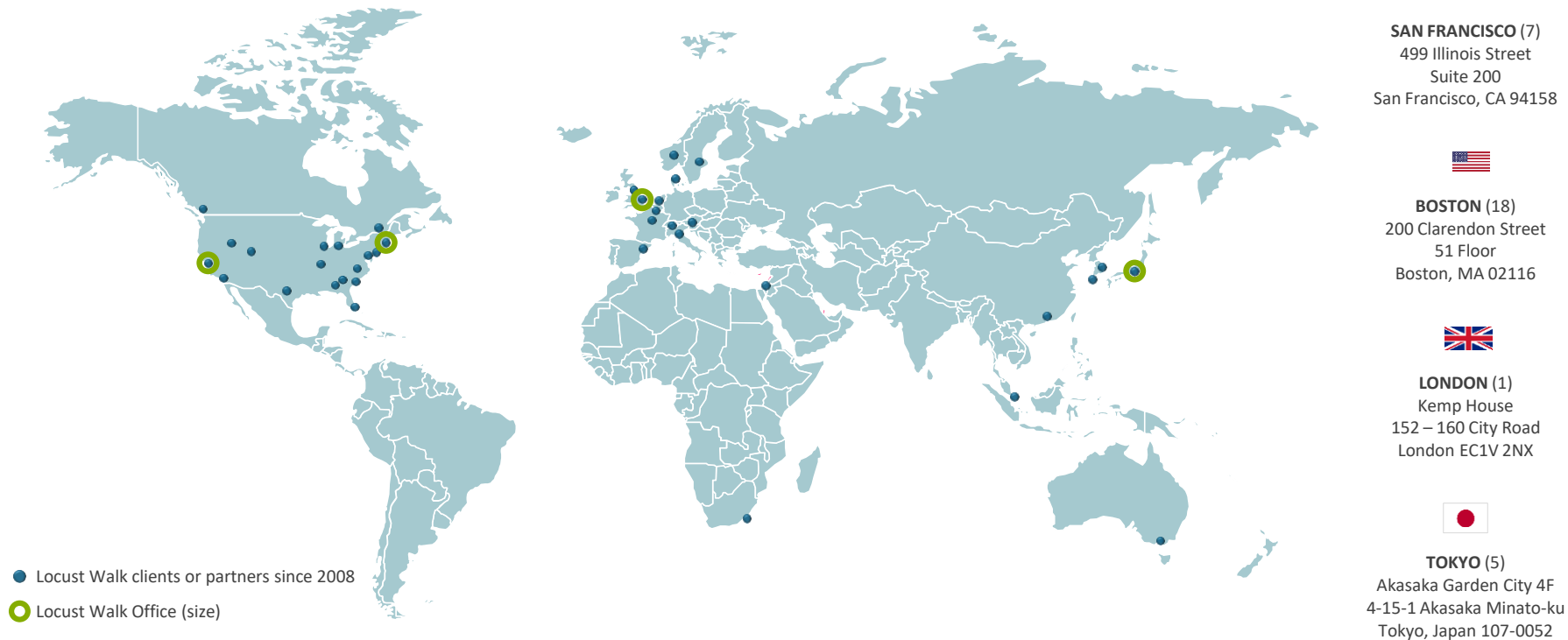
Comprehensive coverage
across biopharma and
medtech segments

- Strong understanding of value drivers, deal structures, and transaction precedents as well as how they differ between the biopharma and medtech segments.
- Biopharma team has completed over 40 transactions at Locust Walk across a range of therapeutic areas, modalities, and all stages of development and marketed products.
- Medtech team brings deep, segment-specific experience from over 25 transactions across various therapeutic areas and care settings for medical device, diagnostics, tools and digital health companies.
- Strong understanding of both the biopharma and medtech segments helps our team identify and maximize the potential of convergence opportunities that many innovative life science companies have top-of-mind.

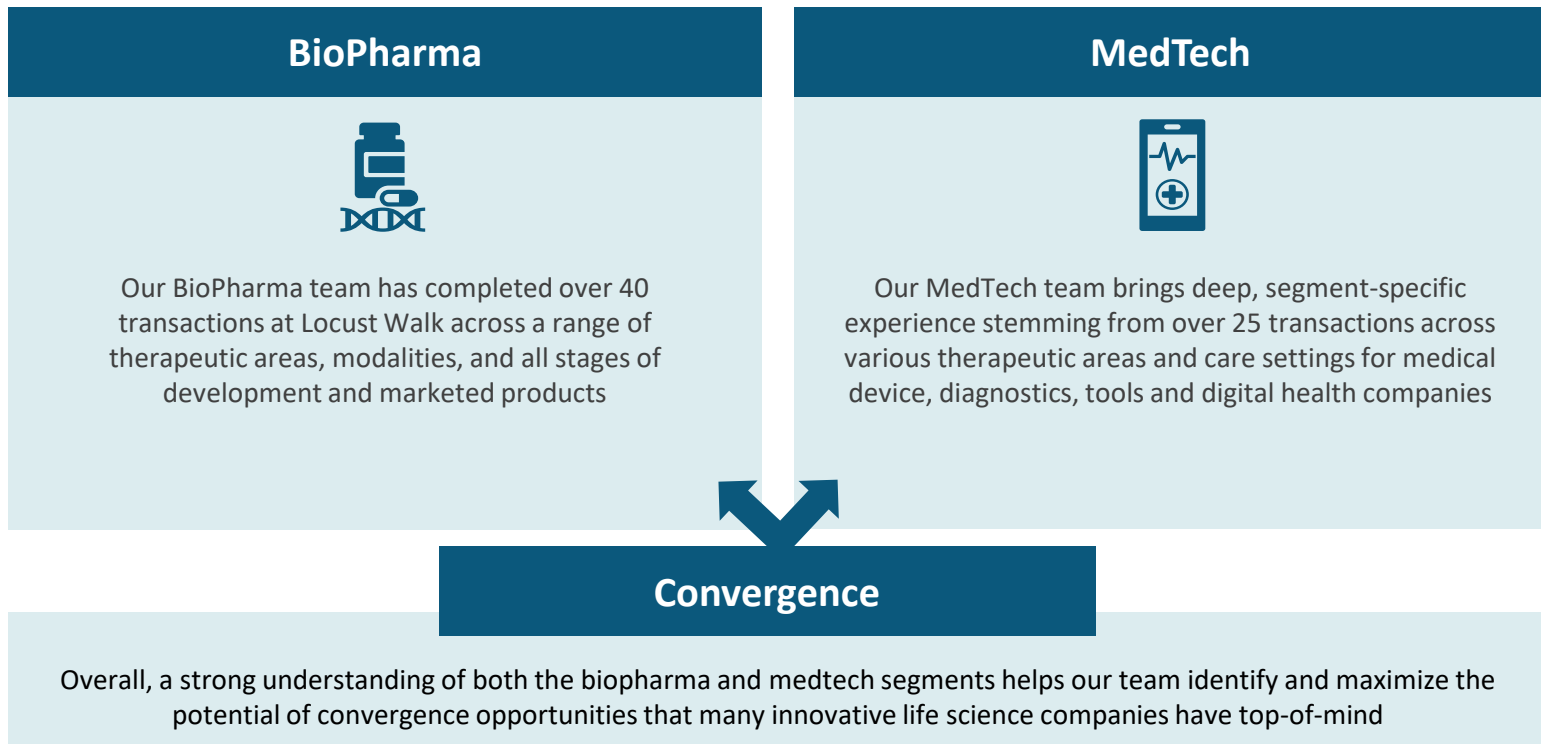
Locust Walk's cohesive combination of strategy, market analytics, and transaction capabilities means that you have one integrated team focused on your entire deal process



Locust Walk maintains a global footprint across all key life science geographies



Locust Walk has a strong understanding of value drivers, deal structures, and transaction precedents as well as how they differ between the biopharma and medtech segments



Locust Walk's leadership team includes successful life science operating, investing, and transaction executives



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