



The State of Emerging Therapeutic Companies June 2023

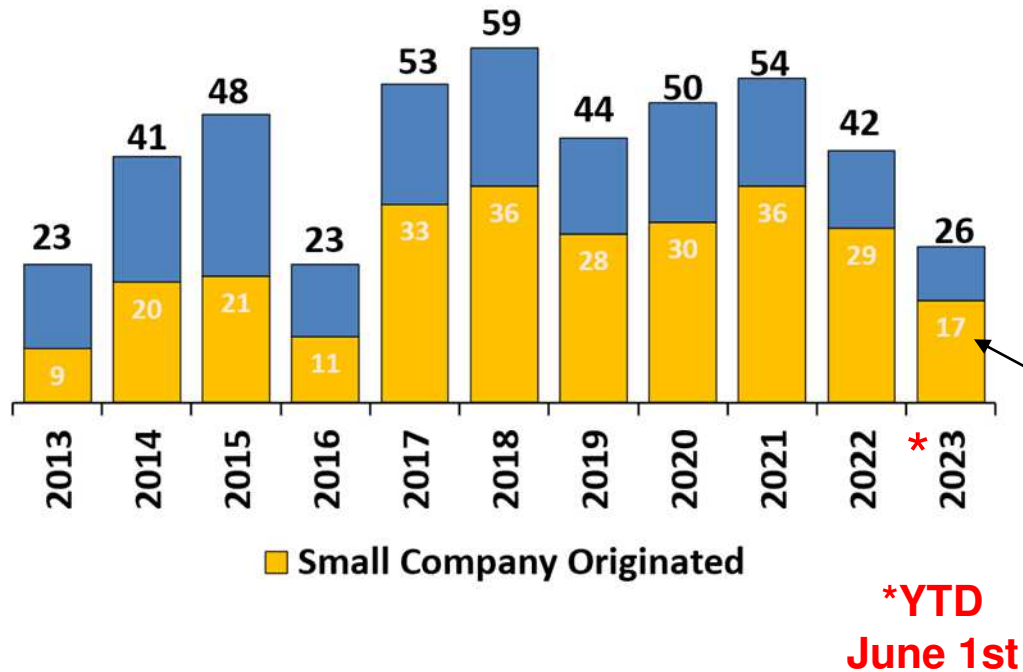
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SVP, Industry Research, BIO**

**Chad Wessel
Director, Industry Research, BIO**

FDA Approvals for Novel Therapeutics

Novel drug approvals ahead of 2022 pace, driven by small companies

26 FDA approvals so far in 2023



2023 YTD Approval Pathways

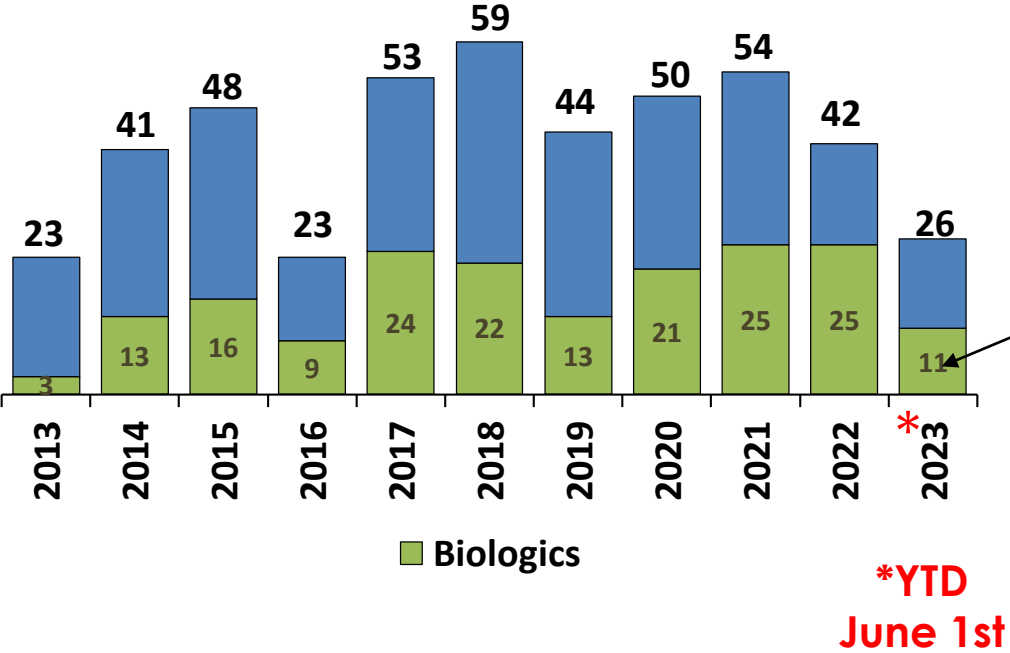
- Accelerated Approvals: 6
- Designation Approvals:
 - Orphan: 11
 - BTDP: 3
 - RMAT: 1
 - QIDP: 1

- **2023 YTD Small company originated: 65%**
- 2013-2015 an average of 44% of approvals originated from a small company
- 2021- May 2023 66% of approvals originated from small companies

FDA Approvals for Novel Therapeutics

Biologics continue to drive precision targeting for drugs and vaccines

11 Biologics approved 2023 YTD



6 protein therapeutics, 2 protein vaccines
1 gene therapy, 1 antisense, 1 microbiome

Drug - Company (Partner or Acquirer)	Type --> Target	Disease
ABRYSVO - Pfizer	Vaccine (protein) --> RSV	RSV
AREXVY - GSK	Vaccine (protein) --> RSV	RSV
VOWST - Seres (Nestle)	Bacteria --> Microbiome (fecal)	C. difficile infection
QALSODY - Ionis (Biogen)	Antisense --> SOD1	ALS (SOD1 gene)
VYJUVEK - Krystal Biotech	Gene Therapy (en vivo) --> collagen VII	Epidermolysis Bullosa (DEB)
EPKINLY - Genmab (Abbvie)	Mab (bispecific) --> CD3/CD20	B-cell Lymphoma (DLBCL)
ZYNYZ - MacroGenics (Incyte)	Mab (full length) --> PD-1	Merkel Cell Carcinoma
LEQEMBI - BioArctic (Eisai)	Mab (full length) --> amyloid-beta	Alzheimer's Disease
ALTUVIIIIO - Amunix (Sanofi)	Protein (fusion) --> Factor VIII	Hemophilia A
ELFABRIO - Protalix (Chiesi)	Enzyme --> α-Galactosidase-A	Fabry Disease (ERT)
LAMZEDE - Zymenex (Chiesi)	Enzyme --> alpha-mannosidase	Lysosomal Storage (ERT)

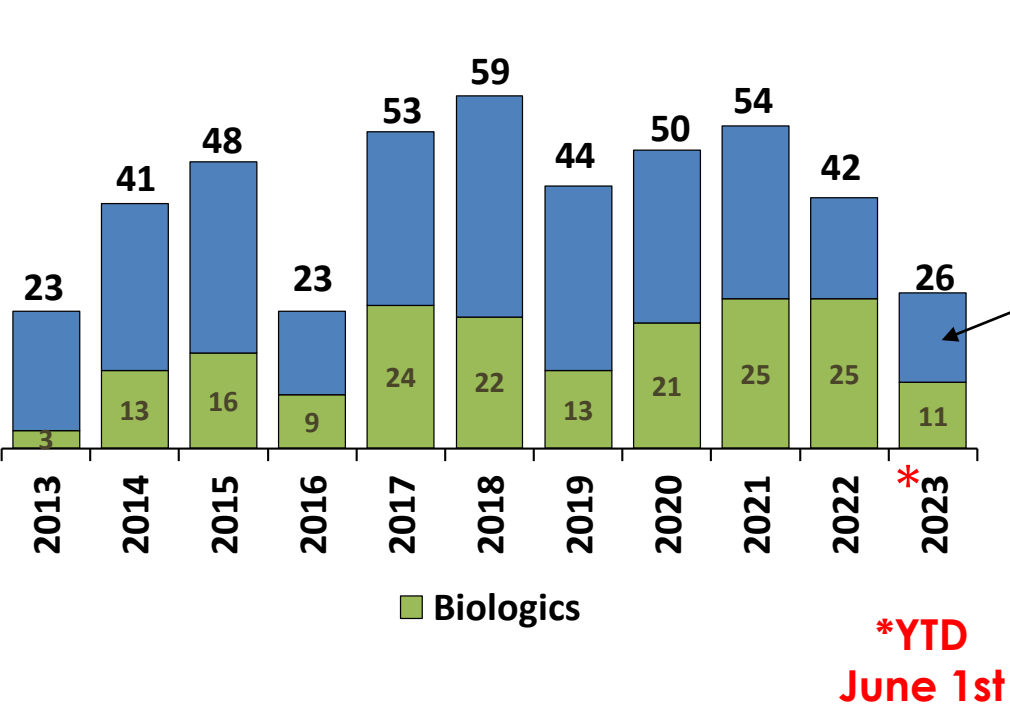
- Since 2013, 180 novel biologics programs have been approved (39%)
- 2013 had the lowest percentage of biologics approvals (13%)
- 2022 had the highest percentage of biologics approvals (60%)
- YTD 2023, 45% of novel approvals have been biologics

FDA Approvals for Novel Therapeutics

Small molecule approvals outpace biologics YTD 2023

15 Small molecule approvals 2023 YTD

4 novel targets



Drug - Company (Partner or Acquirer)	Type --> Target	Disease
VEOZAH - Ogeda (Astellas)	Small Molecule --> NK3 receptor	Hot Flashes (Menopause)
SKYCLARYS - Reata	Small molecule --> Nrf2	Friedreich's Ataxia
JESDUVROQ - GSK	Small molecule --> prolyl hydroxylase	Anemia due to CKD
PAXLOVID - Pfizer	Small molecule --> 3CL protease (Cov2)	COVID-19
DAYBUE - Neuren (ACADIA)	Small molecule --> unknown	Rett Syndrome
MIEBO - Novaliq (Bausch)	Small Molecule --> unknown	Dry Eye Disease
ZAVZPRET - BMS (Pfizer)	Small molecule --> CGRP Receptor	Migraine
ORSERDU - Eisai (Menarini)	Small molecule --> estrogen receptor	Breast Cancer
JAYPIRCA - Redx (Eli Lilly)	Small molecule --> BTK	Mantle Cell Lymphoma
JOENJA - Novartis (Pharming)	Small molecule --> PI3K	Activated PI3K (APDS)
XACDURO - Entasis (Innoviva)	Small molecule --> β-lactamase	A. Baumannii infection
REZZAYO - Cidara (Melinta)	Small molecule --> β-Glucan Synthase	Candida infection
FILSPARI - BMS (Traverse)	Small molecule --> ang + endothelin R	IgA Nephropathy
BRENZAVVY - TheracosBio	Small Molecule --> SGLT-2	Type 2 Diabetes
INPEFA - Lexicon	Small Molecule --> SGLT-1/2	Heart Failure

Clinical Pipeline

Clinical Pipeline increased 2.8% vs. May 2022

6,918 programs in 2022
7,111 programs in 2023* (+2.8%)

>80% of Pipeline is early-stage
(Phase 1/2) due to Oncology

"Other" Category
Dermatology
Allergy
Renal
Gastroenterology
Rheumatology (non autoimmune)
Urology
Obstetrics/Gynecology

Disease	Total	%	P1	P2	P3	NDA & BLA
Oncology	3150	44%	1208	1610	299	33
Neurology	712	10%	229	322	148	13
Infectious Disease	659	9%	231	261	146	21
Immunology	449	6%	116	203	110	20
Endocrine	326	5%	108	162	45	11
Metabolic	263	4%	76	113	61	13
Ophthalmology	259	4%	26	152	66	15
Cardio	186	3%	39	90	51	6
Psychiatry	181	3%	59	77	36	9
GI	174	2%	50	89	29	6
Respiratory	154	2%	47	76	31	0
Hematology	126	2%	27	52	37	10
Other	472	7%	112	250	94	16
Total	7111	NA	2328	3457	1153	173
Percent	100%	100%	33%	49%	16%	2%

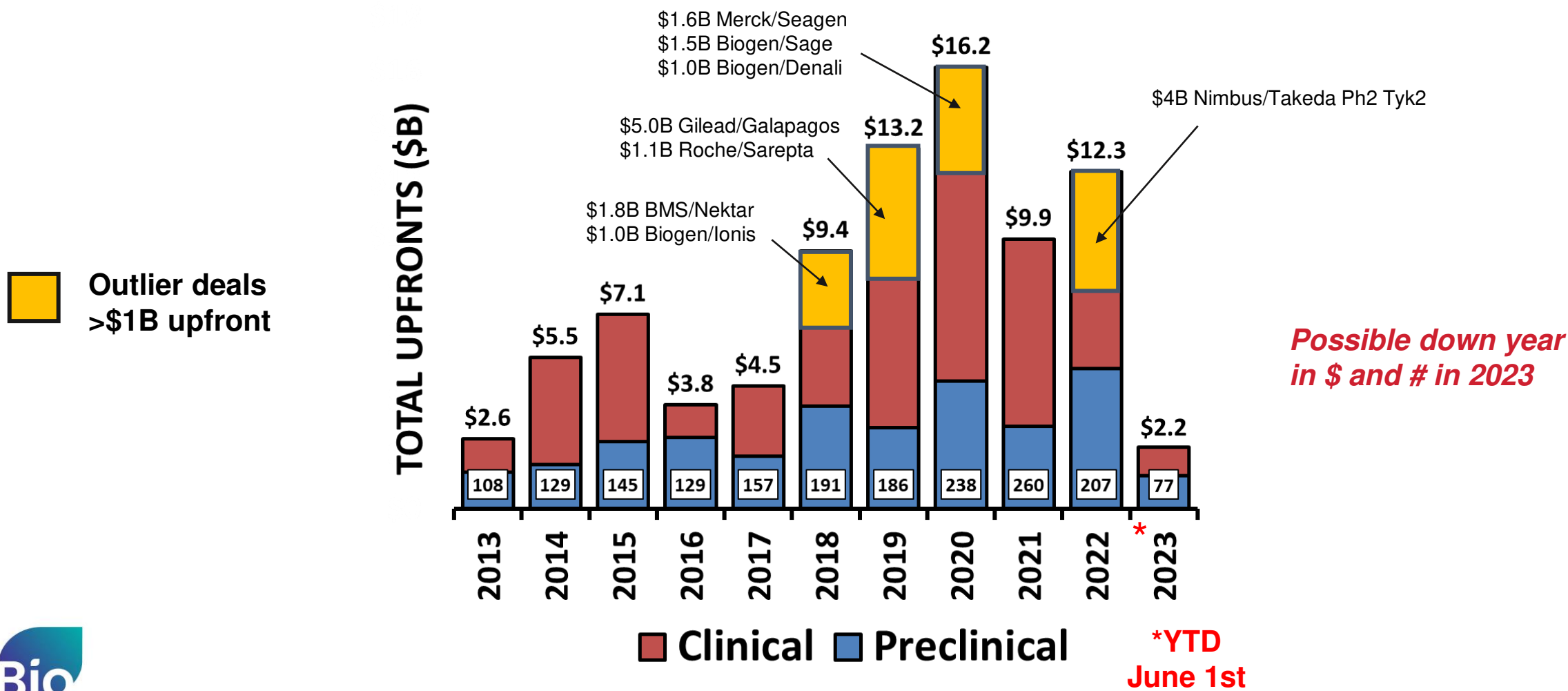


* Company drug-indication clinical programs intended to eventually reach FDA approval (Data as of May 2023)

Out-Licensing

R&D-stage drug asset licensing declining in 2023

Upfront payments to emerging companies for pipeline assets



Out-Licensing

Asian deals lead top 10 clinical-stage deals, all early-stage

Top 10 clinical-stage deals of 2023 YTD by potential payout

Licensors/Licensee	Licensors Location	Stage	Area / Assets	Upfront (\$M)	Potential (\$B)
Eisai <-- Bliss Bio	ASIA	P2	ADC - anti-HER2	ND	\$2.0
BioNTech <-- DualityBio	ASIA	P2	ADC - Solid Tumors (2)	\$170	\$1.7
Lilly <-- Confo	Europe	P1	Small molecule --> AT2R GPCR (Pain)	\$40	\$1.2
AZ <-- Keymed/KYM	ASIA	P1	ADC - anti-Claudin 18.2	\$63	\$1.2
Janssen <-- Pipeline	USA	P1	Small mol --> muscarinic M1 receptor (Neuro)	\$75	\$1.1
Sanofi <-- Maze	USA	P1	Small mol --> glycogen synthase (Pompe's)	ND	\$0.8
Corbus <-- CSPC	ASIA	P1	ADC - anti-Nectin-4	\$8	\$0.7
Roche <-- Zion Pharma	ASIA	P1	Small mol (TKI) --> HER2	\$70	\$0.6
Lighthouse <-- Quince	USA	P1	Small mol --> lysine-gingipain (4) (Alzheimer's)	ND	\$0.6
Cullinan <-- Harbour BioMed	ASIA	P1	Bispecific - B7H4 x 4-1BB	\$25	\$0.6
Janssen <-- Cellular Biomedicine	USA	P1	CAR-Ts (NHL)	\$245	ND
BioNTech <-- OncoC4	USA	P2	Mab anti-CTLA4 (Solid Tumors)	\$200	ND

Majority of deals are <\$100M upfront, except Duality, Cellular, OncoC4



Out-Licensing

Top preclinical deals mostly USA-based, mostly biologics

Top 10 Preclinical-stage deals of 2023 YTD by potential payout

Licensor <-- Licensee	Licensor Location	Stage	Area: Assets	Upfront (\$M)	Potential (\$B)
Neurocrine <-- Voyager	USA	PC	Gene Therapy: GBA1 Parkinson's + 3 (4)	\$175	\$4.4
Genentech <-- Belharra	USA	PC	photoaffinity-based chemoproteomics (multi)	\$80	\$2.1
Novo <-- Life Edit (ElevateBio)	USA	PC	Gene Editing (7) (rare & cardio)	ND	\$1.9
Moderna <-- Generation Bio	USA	PC	ctLNP delivery of ceDNA (3) (Immune/Liver)	\$76	\$1.9
Novartis <-- Bicycle	USA/Europe	PC	Radiopeptides (2) (Oncology)	\$50	\$1.7
Bayer <-- Bicycle	USA/Europe	PC	Radiopeptides (3) (Oncology)	\$45	\$1.7
Lilly <-- Scribe	USA	PC	Gene editing (Neuro)	\$75	\$1.6
GSK <-- WuXi Biologics	ASIA	PC	Mabs (4) (Oncology)	\$40	\$1.5
AbbVie <-- Immunome	USA	PC	Target ID (10) (Oncology)	\$30	\$1.3
Moderna <-- CytomX	USA	PC	mRNA masking (via probody peptide, multi)	\$35	\$1.2

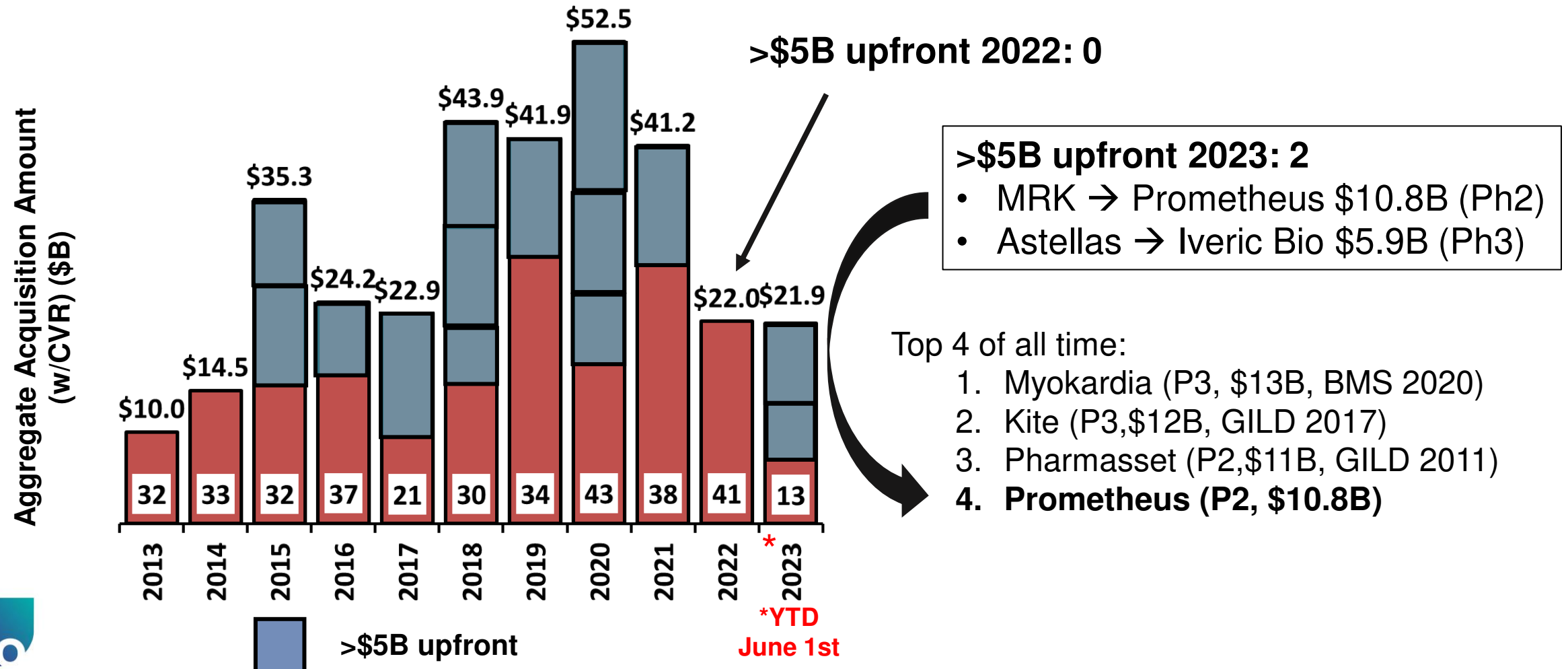
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Acquisitions of R&D-stage BioPharma

Acquisitions of pre-market companies pick up in Spring 2023

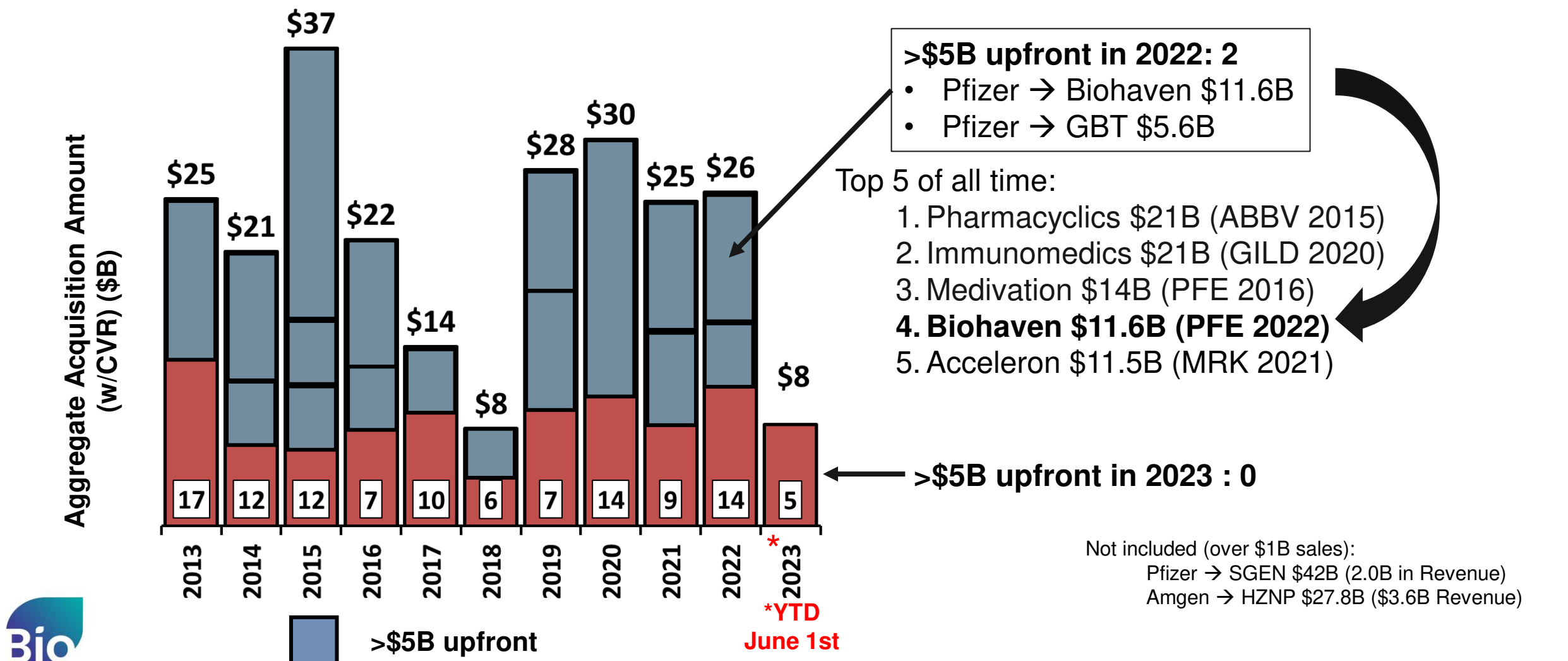
2023 > 2022 in Total Dollar Amount



Acquisitions of Market-Stage BioPharma with <\$1B Sales

Post Pfizer 2022, mostly sub-\$5B market-stage acquisitions

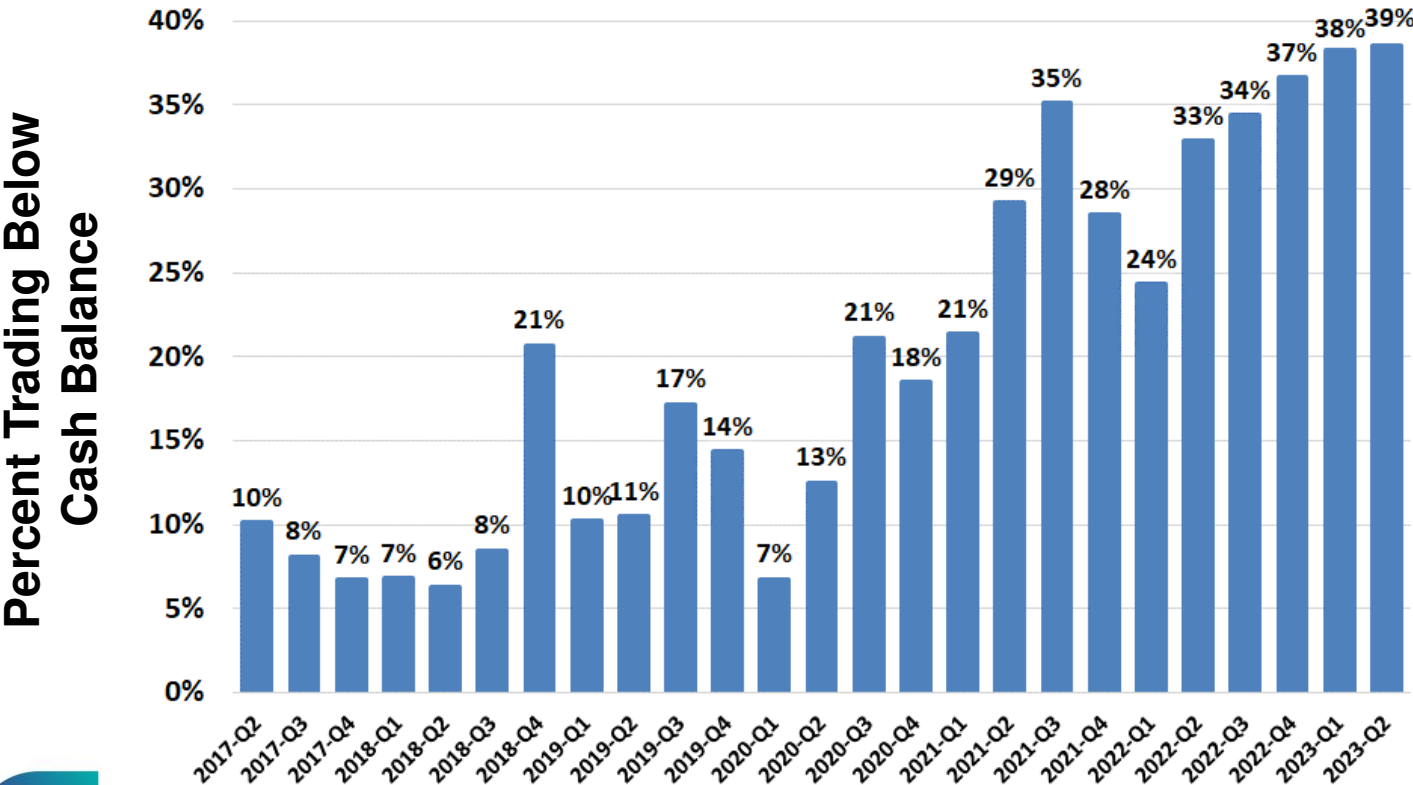
Below average dollar volume YTD



Biotech Valuations

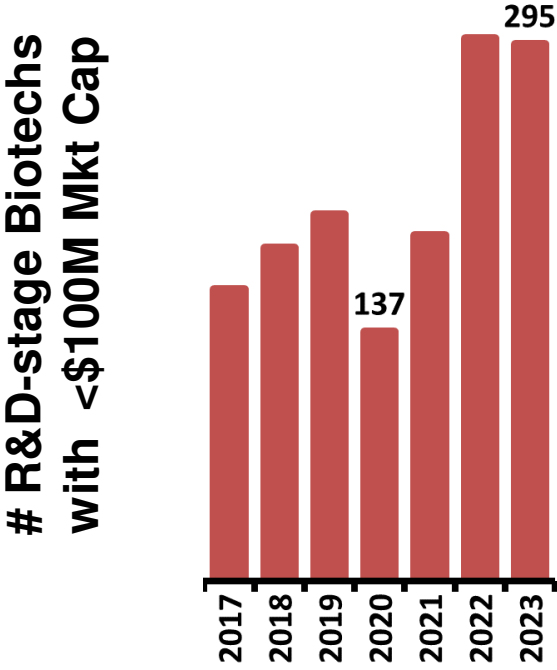
39% of small biotechs trade under cash balance

Record Number of Small Companies* Trading Below Cash



* U.S. Companies with <500 FTEs
Current Market Cap (or end of Q) vs prior Q Cash

Nearly Half of R&D-stage Companies Trade under \$100M

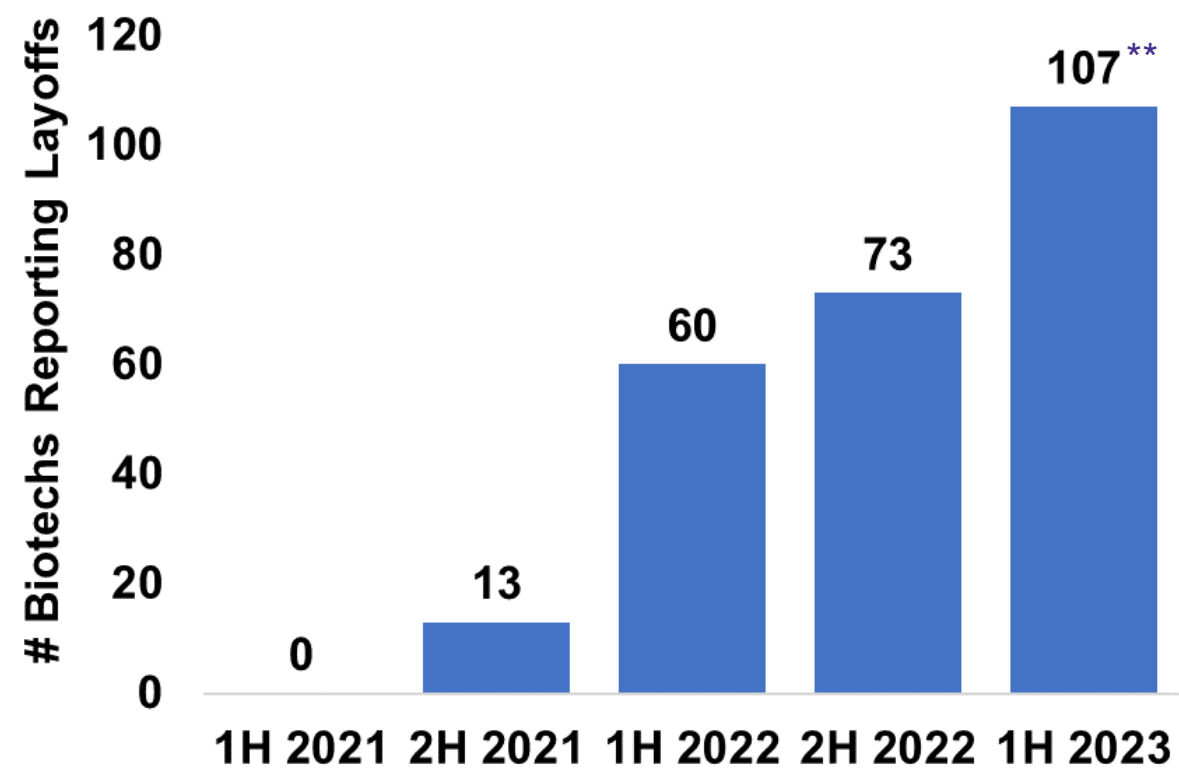


Year end low of 137 in 2020



Biotech Layoffs

Double the pace in 2023 for BioPharma Layoff announcement



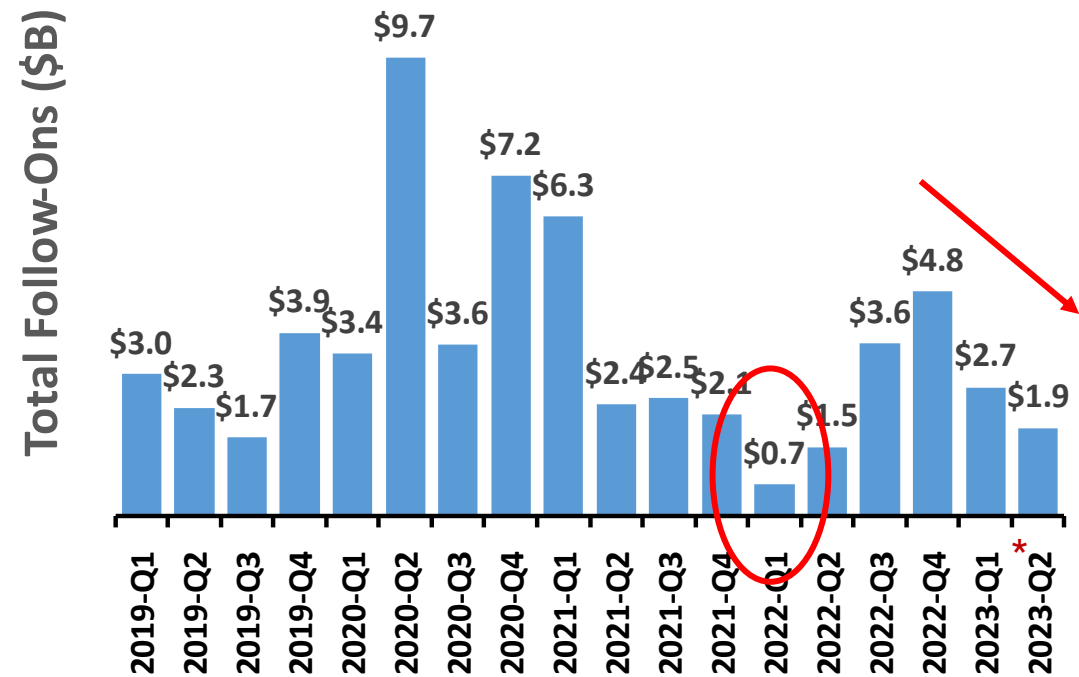
**As of May 25th



Follow-On Offerings

Most R&D-Stage U.S. companies struggle to raise capital

Follow-on rebound in late 2021 has not gained momentum
S&P Biotech Index Fund (XBI) is also sideways, recovering from SVB drop



* as of
June 1st



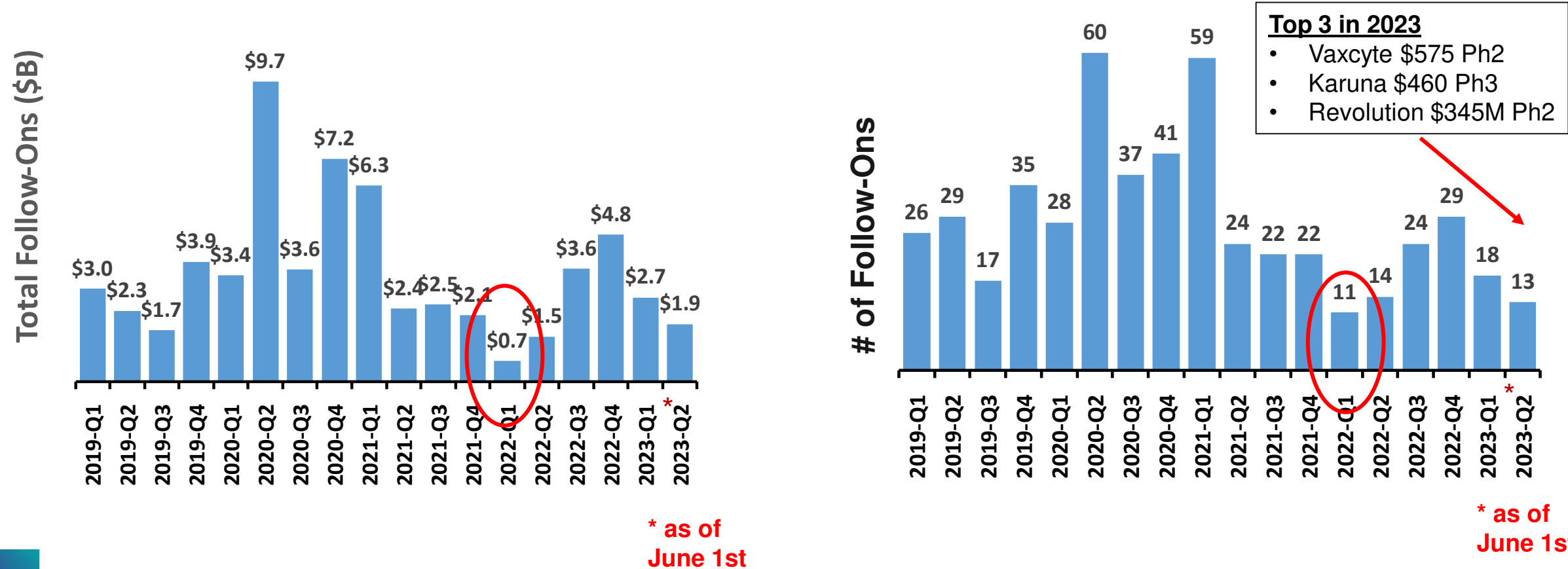
Follow-on lows steeper than XBI lows



Follow-On Offerings

Most R&D-Stage U.S. companies struggle to raise capital

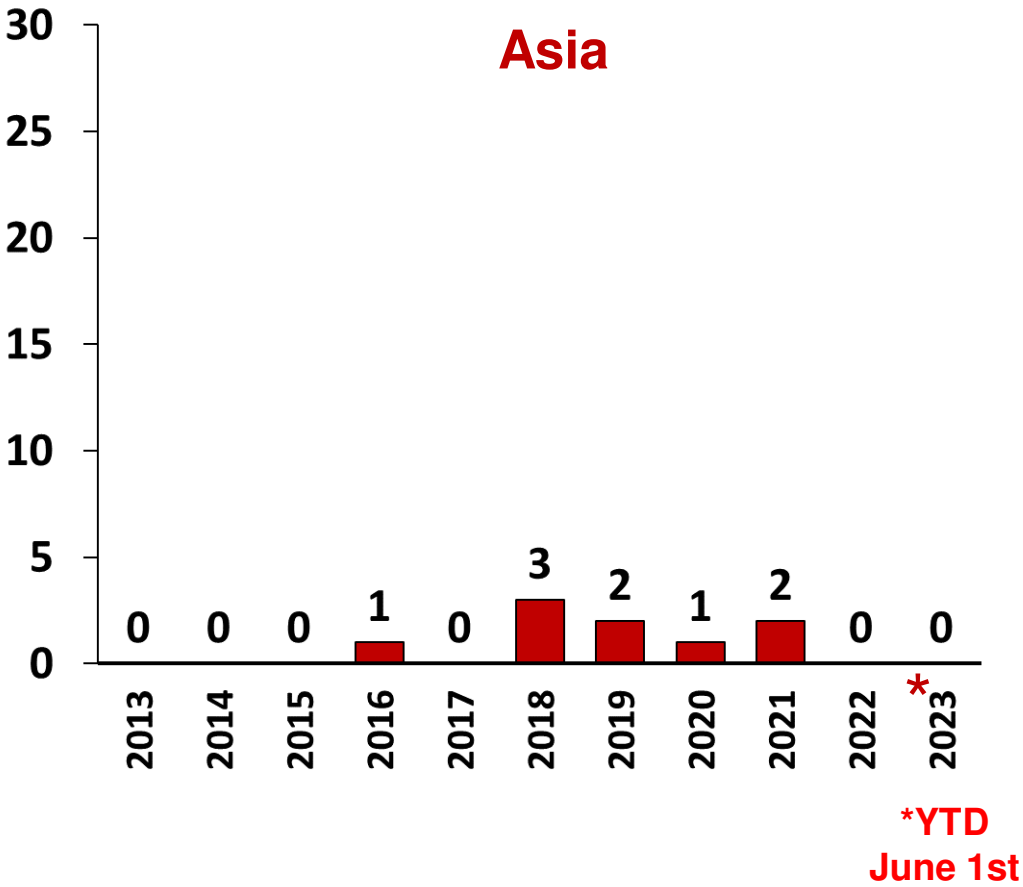
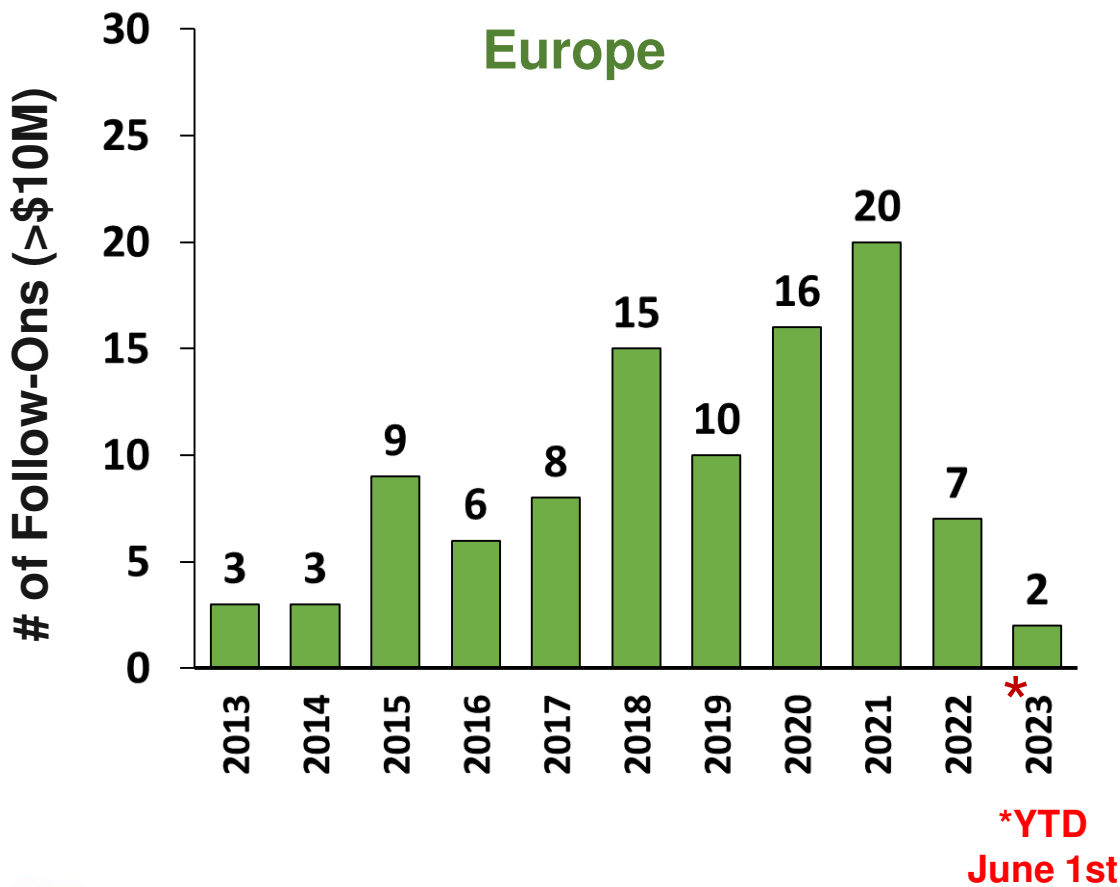
Companies with solid clinical data can raise via follow-on offerings



Follow-On Offerings

Very few R&D-Stage Ex-U.S. companies raising funds via secondary offerings

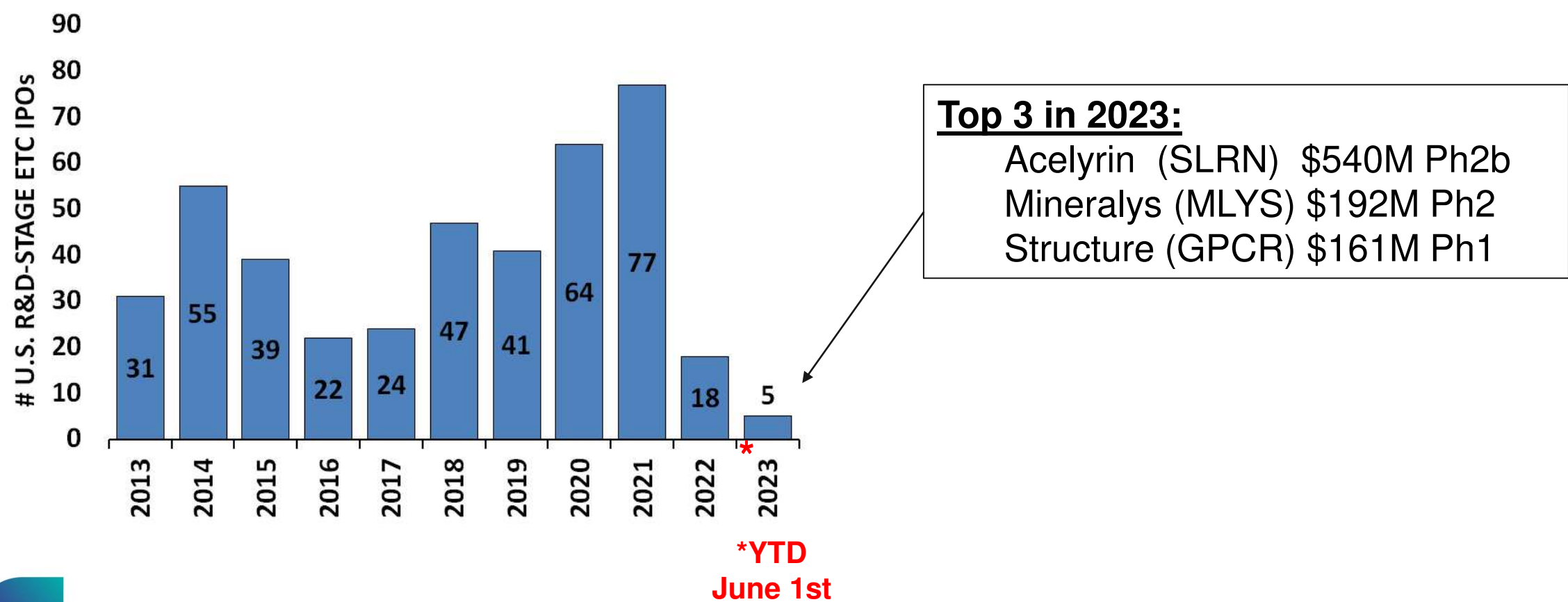
European offerings drop significantly from Covid highs



Initial Public Offerings

IPOs from R&D-Stage U.S. companies declining, with exceptions

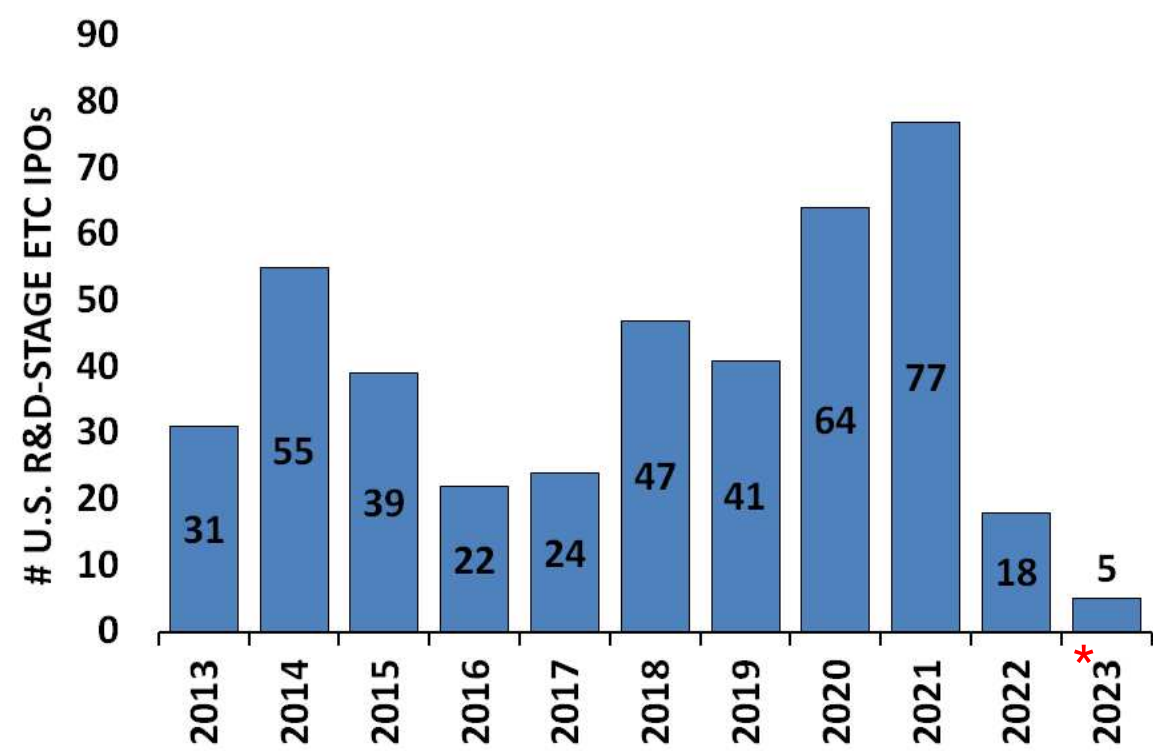
IPOs from US-based Companies



Initial Public Offerings

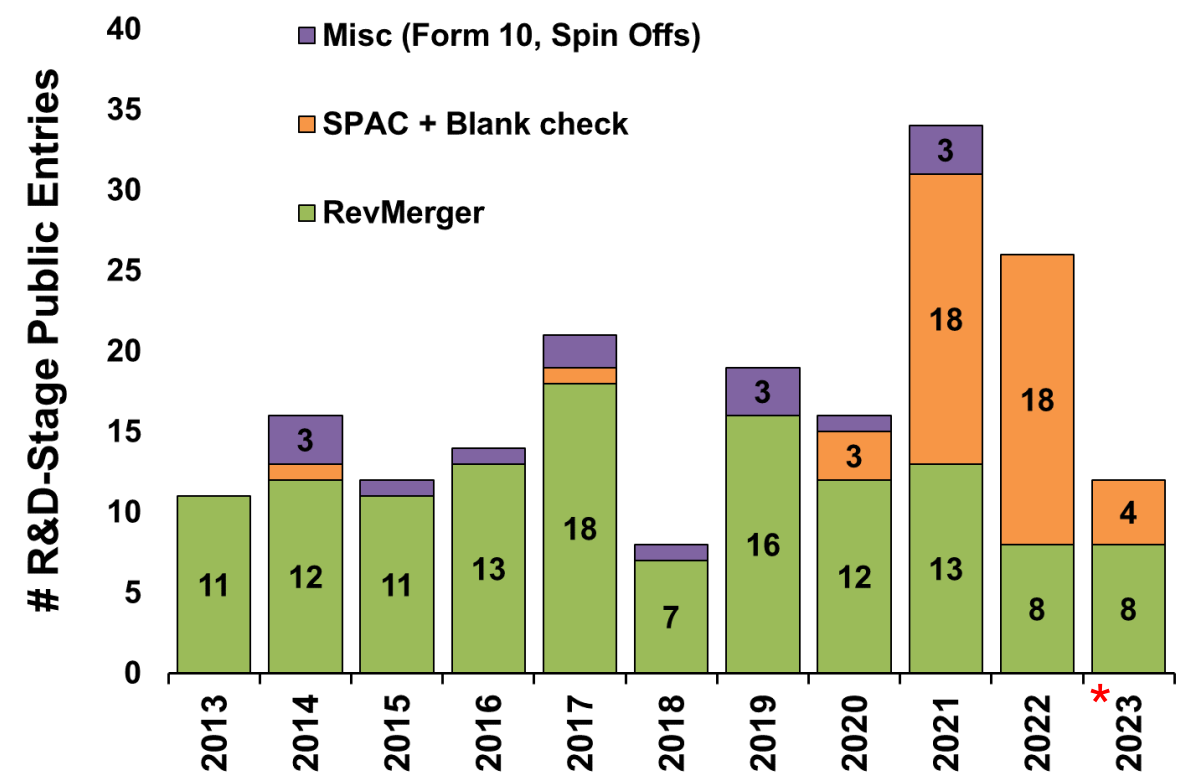
IPOs from R&D-Stage U.S. companies declining, with exceptions

IPOs from US-based Companies



*YTD
June 1st

Alternative Market Entry

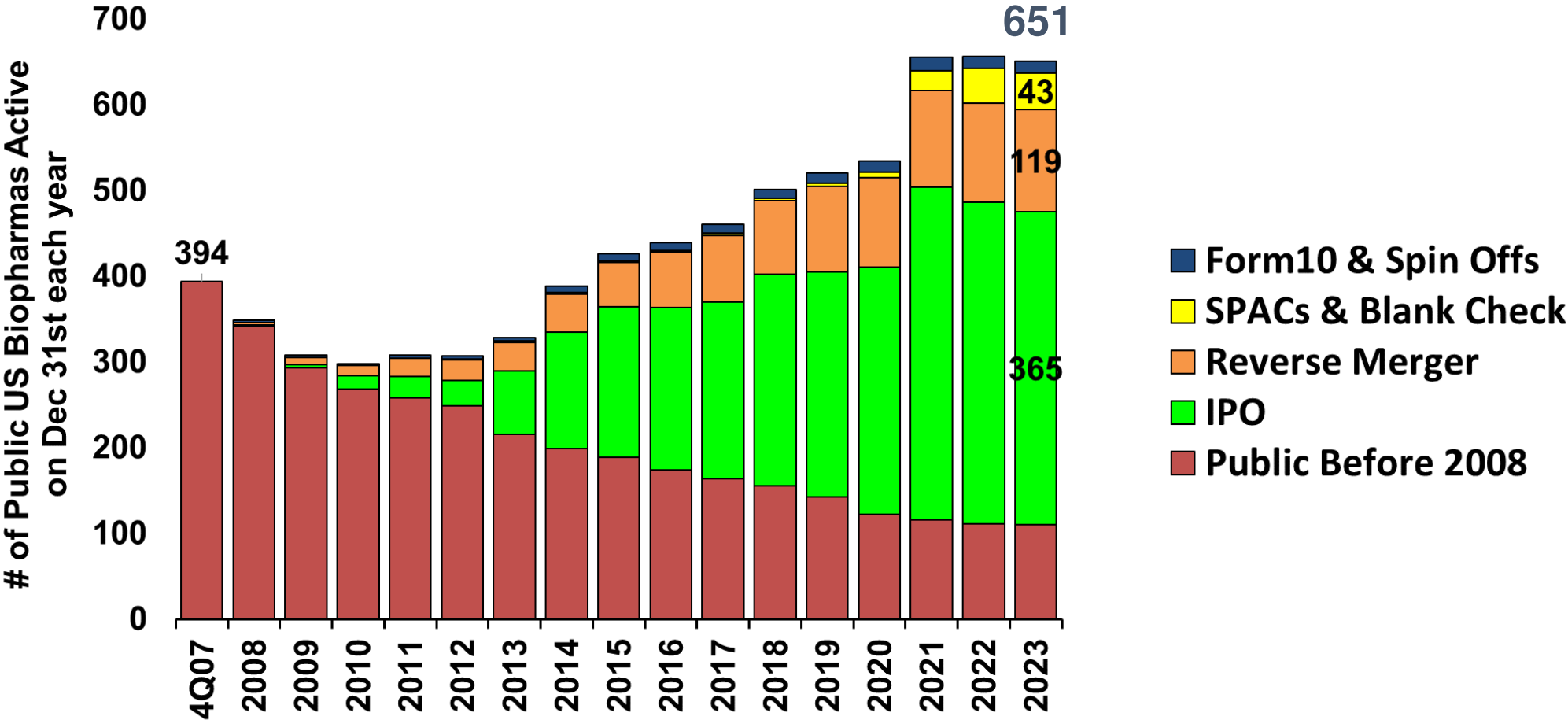


*YTD
June 1st

Public Companies

83% of U.S. publicly traded Biopharma companies debuted in last 10 years

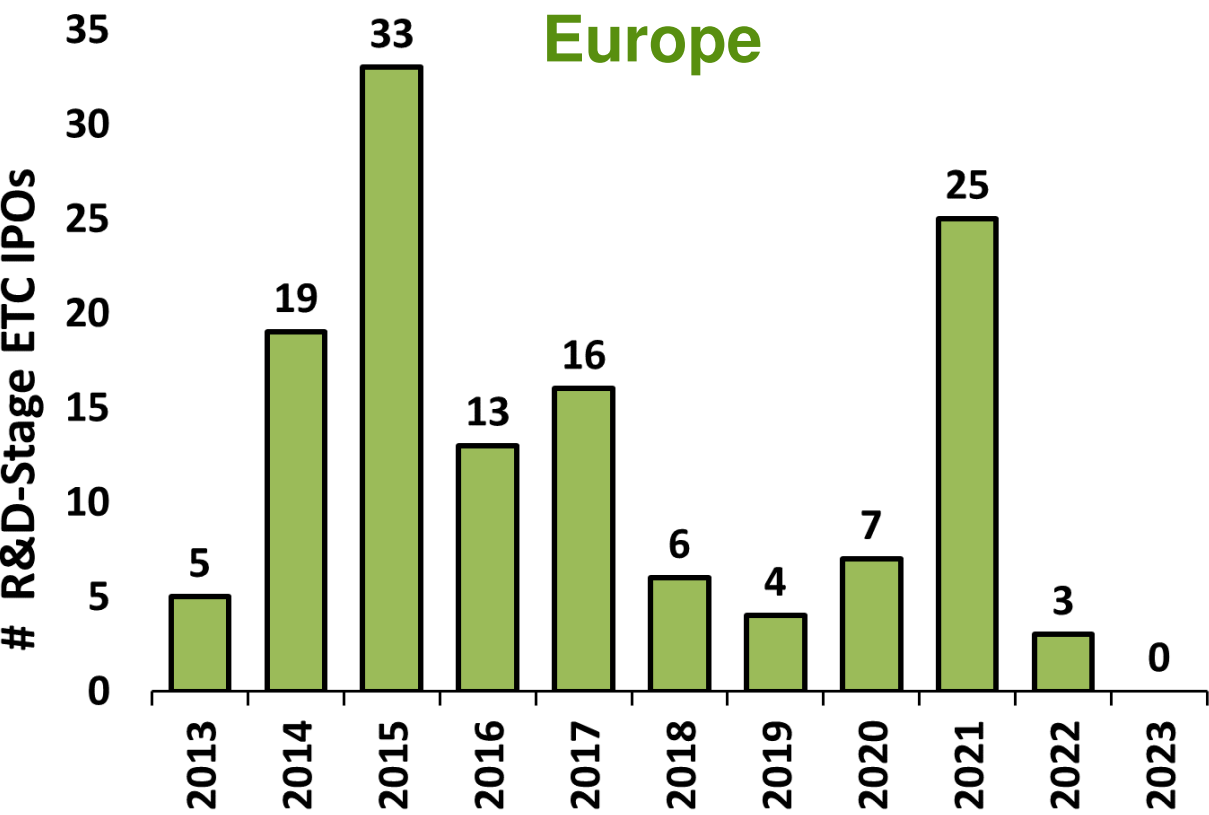
Number of traded U.S. Biopharmas since 2007



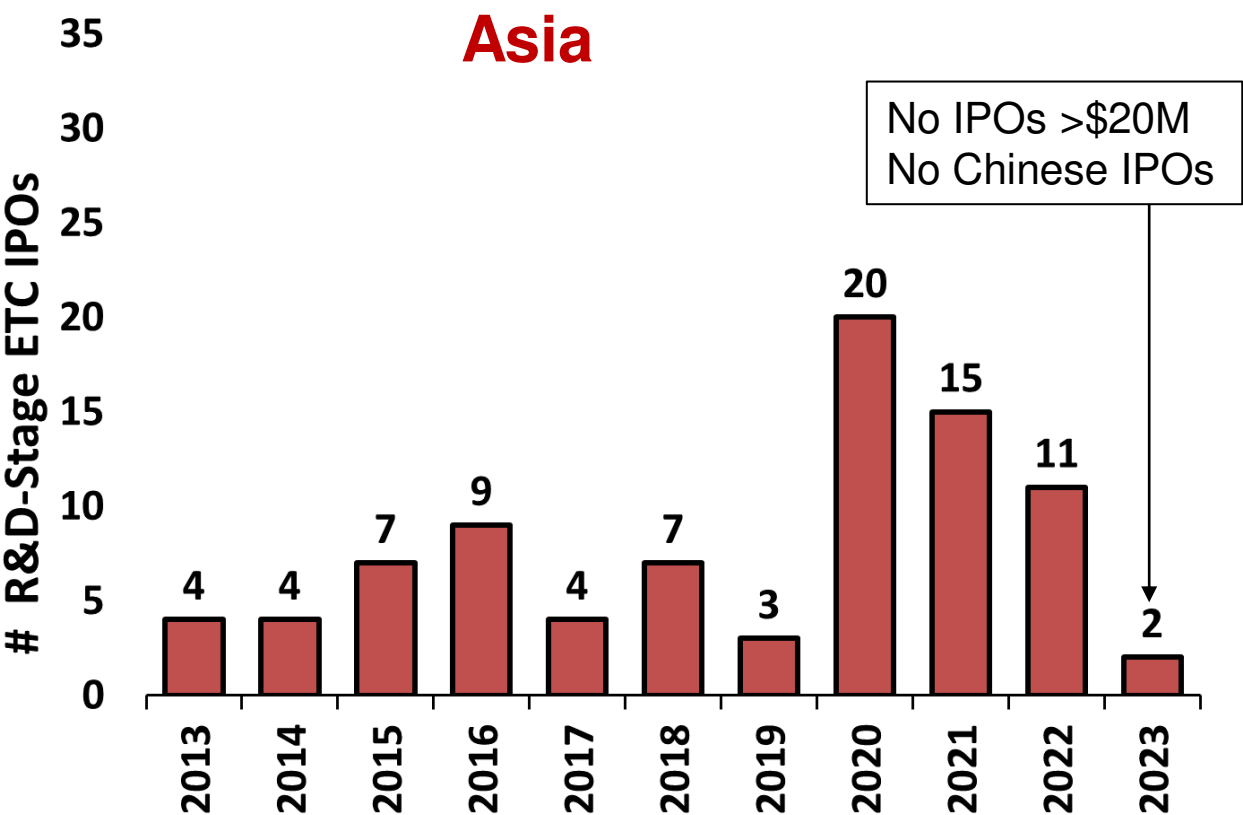
Initial Public Offerings

IPO window closed for R&D-Stage Ex-U.S. companies

2022 was lowest 10 years for Europe, 2023 worse



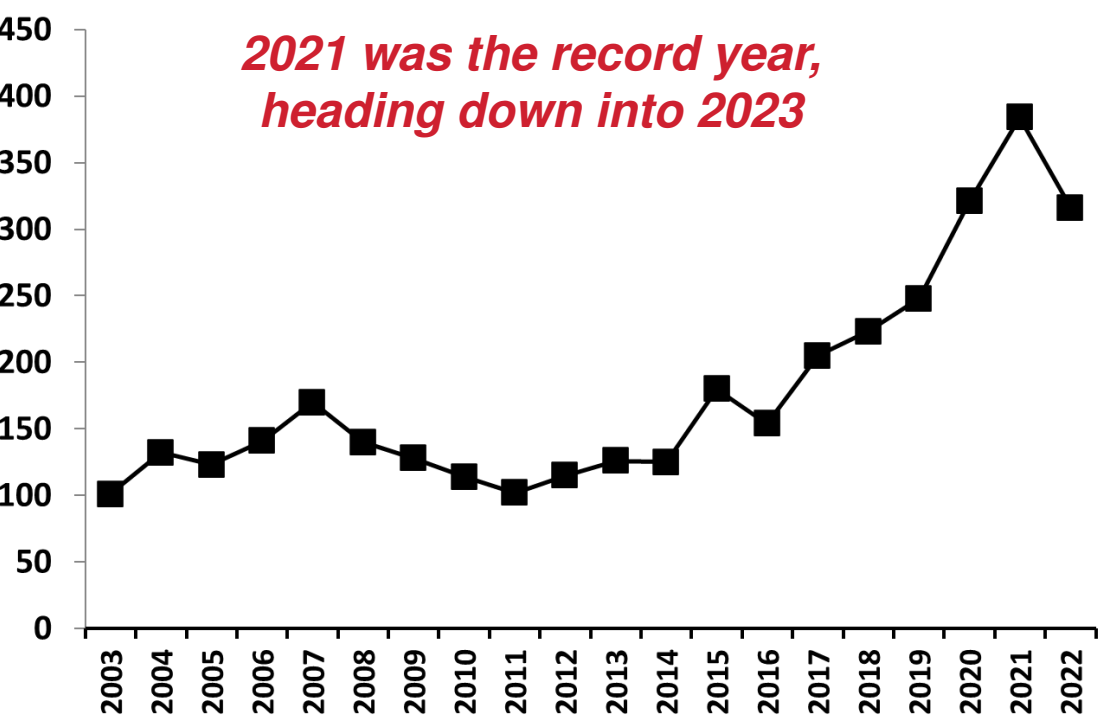
Asia back to Pre-Covid levels



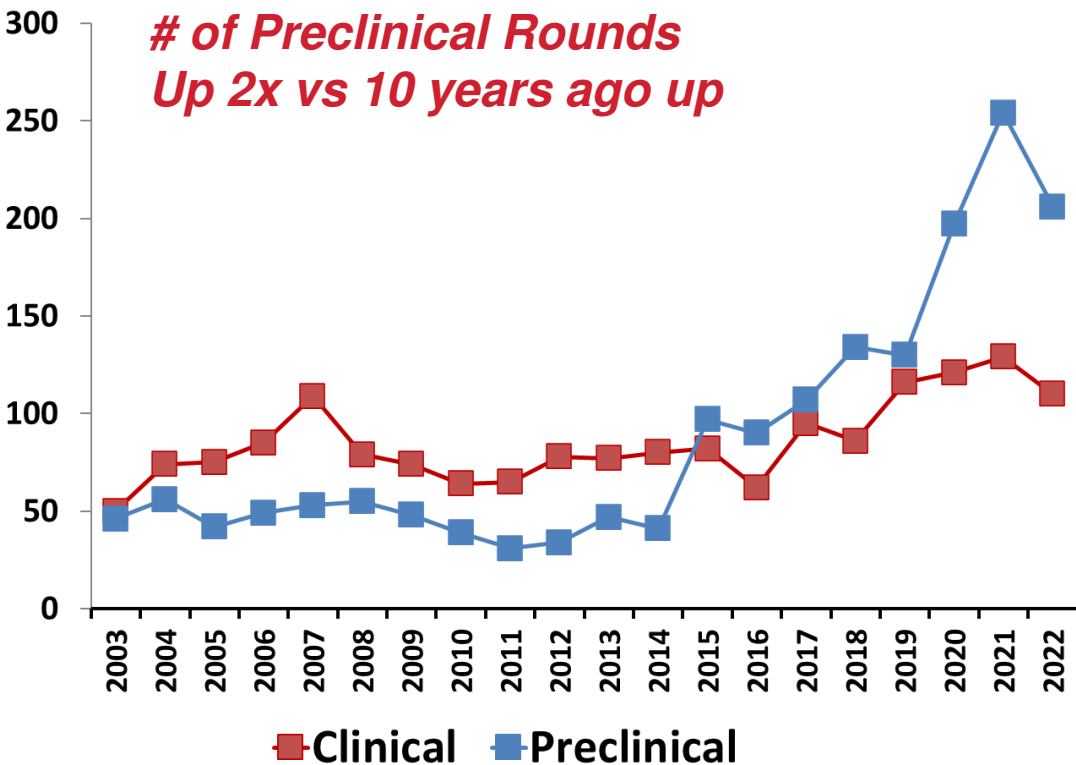
Venture Capital

Number of U.S. VC rounds likely to drop for second year

of \$10M+ rounds on declining



...for both clinical and preclinical companies



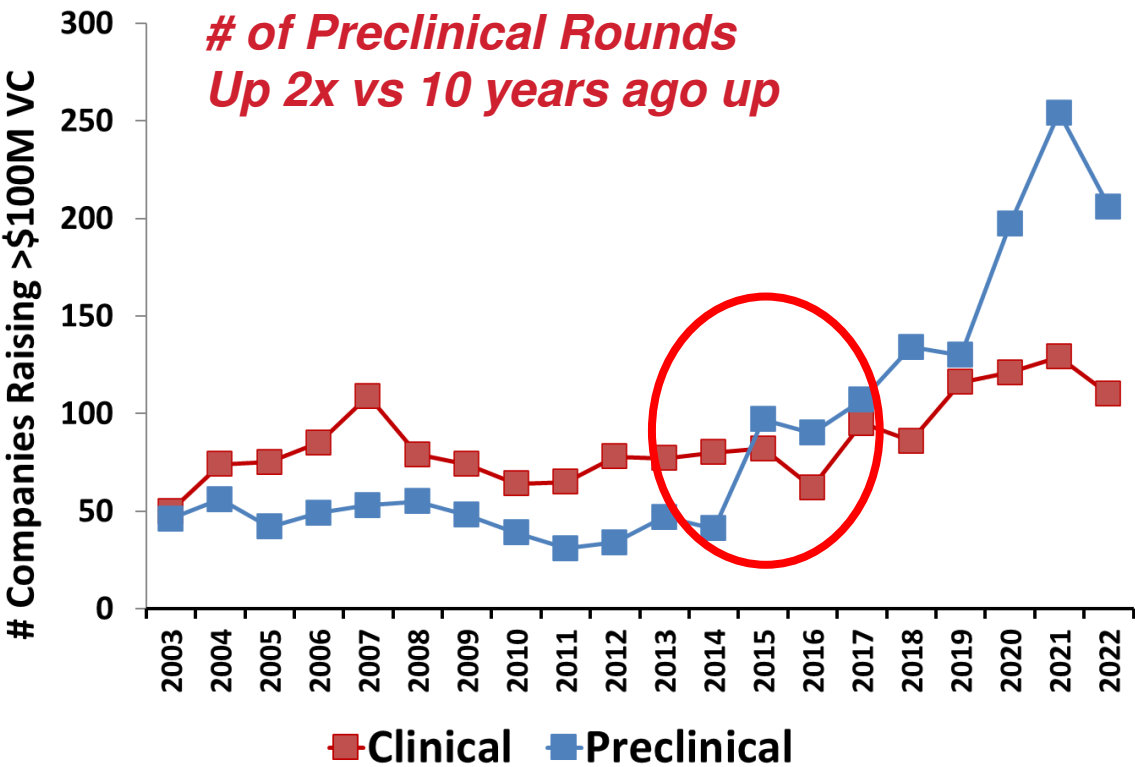
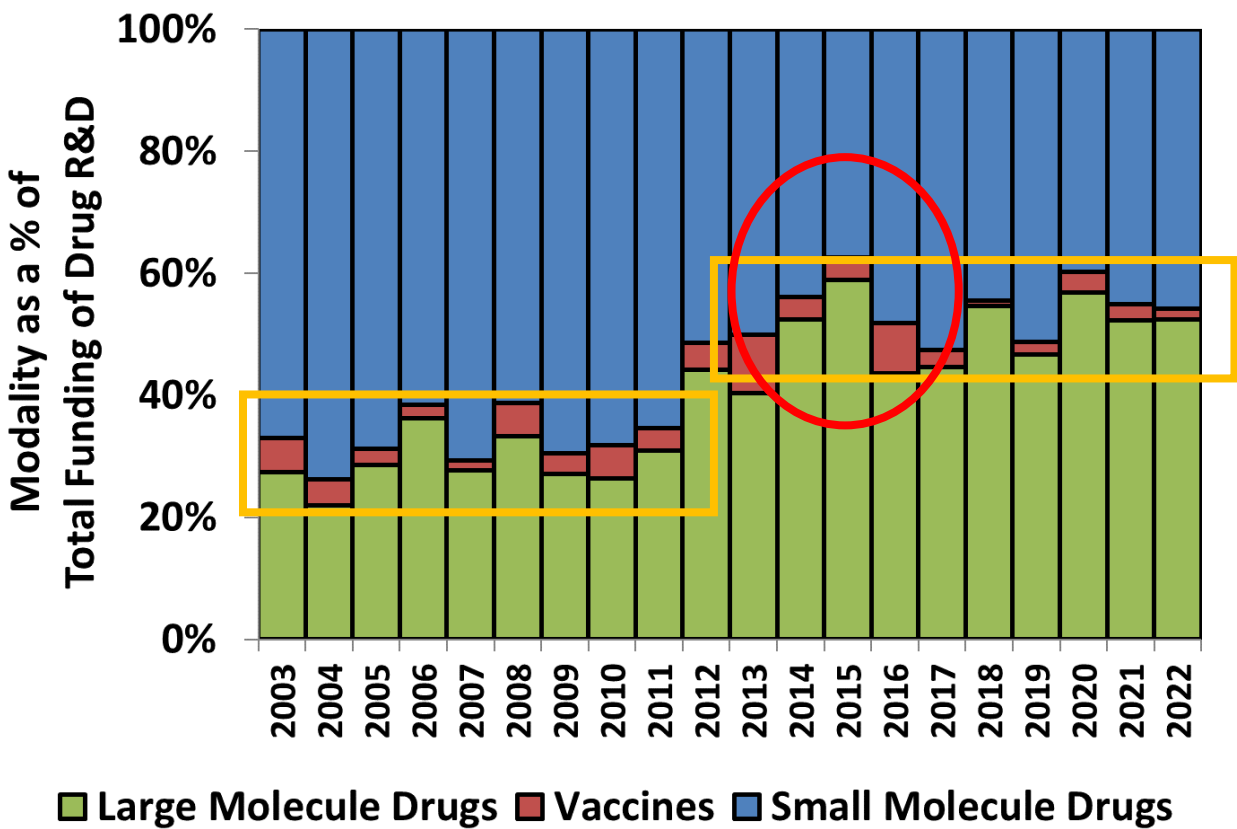
63
Q1
2023



Venture Capital

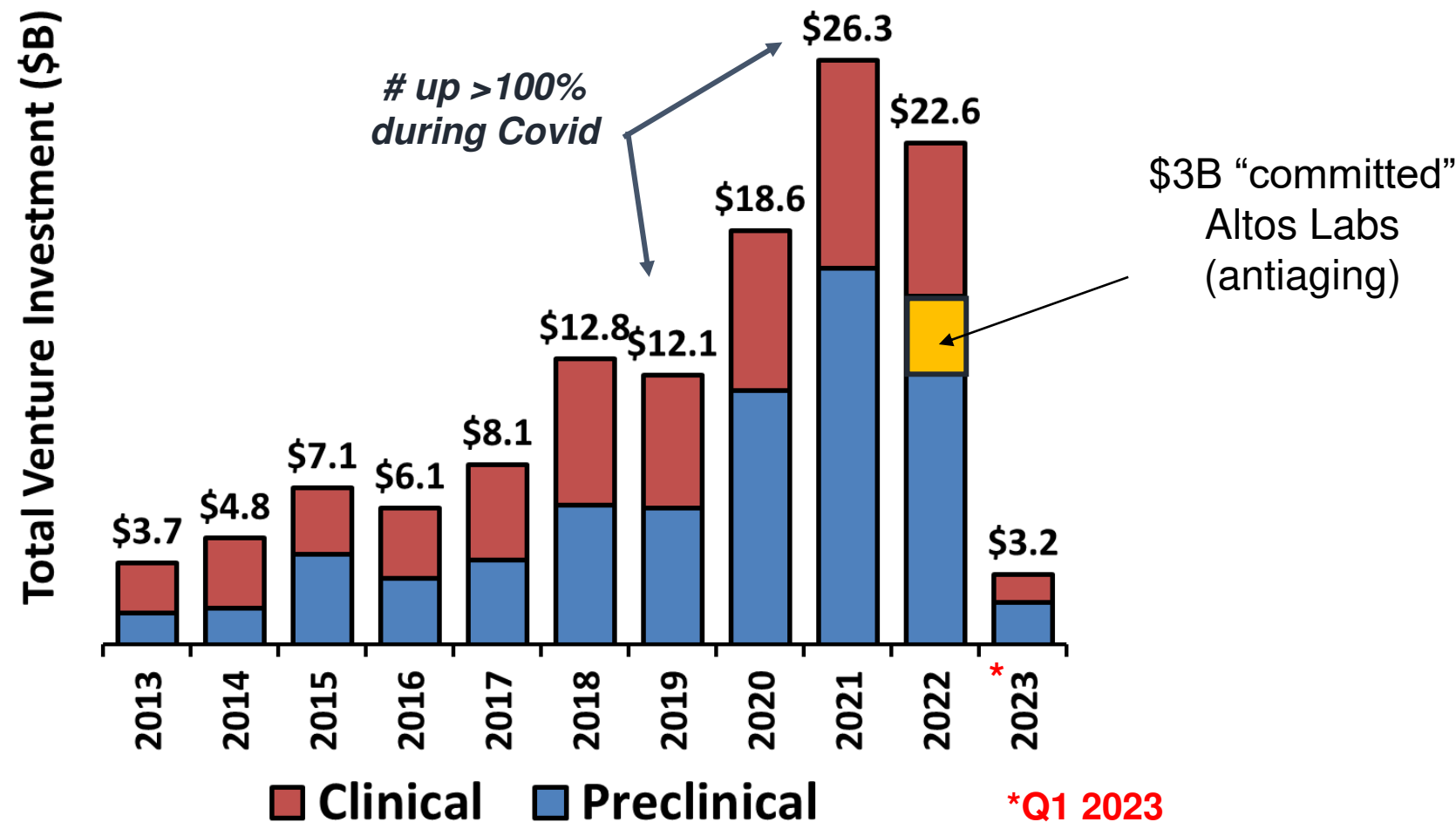
Biologics remain in focus since 2015 peak

Biologics remain at 50% of Venture Capital



Venture Capital

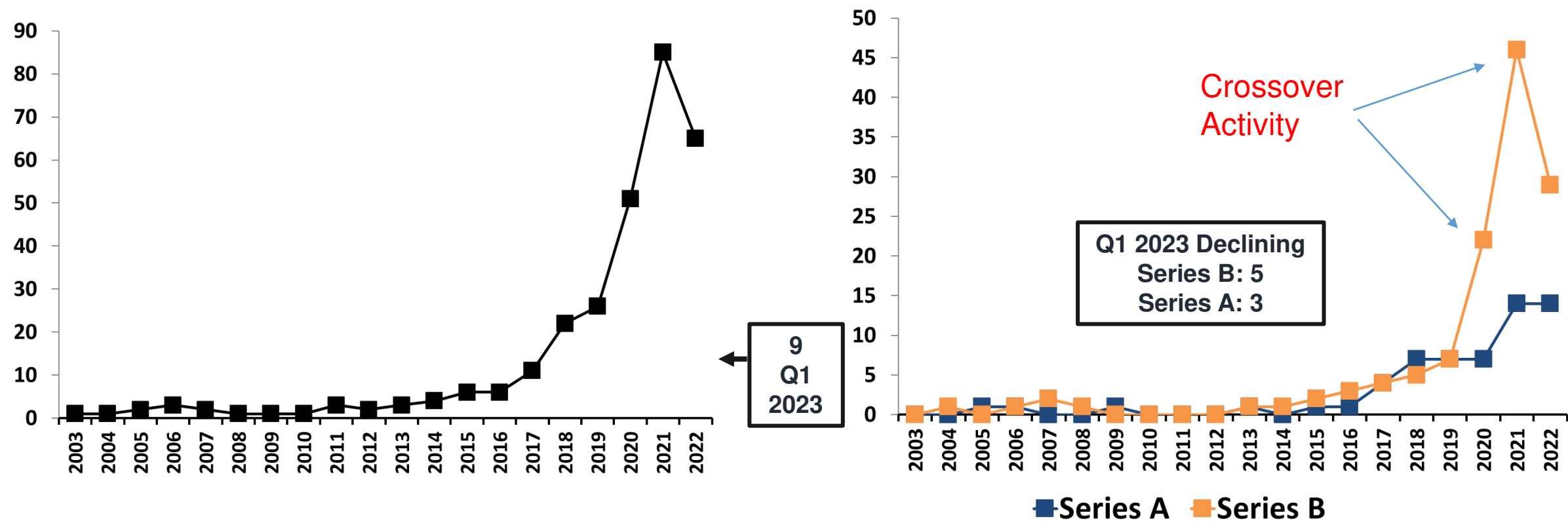
U.S. venture capital reached its peak in 2021



Venture Capital

Large crossover rounds declining

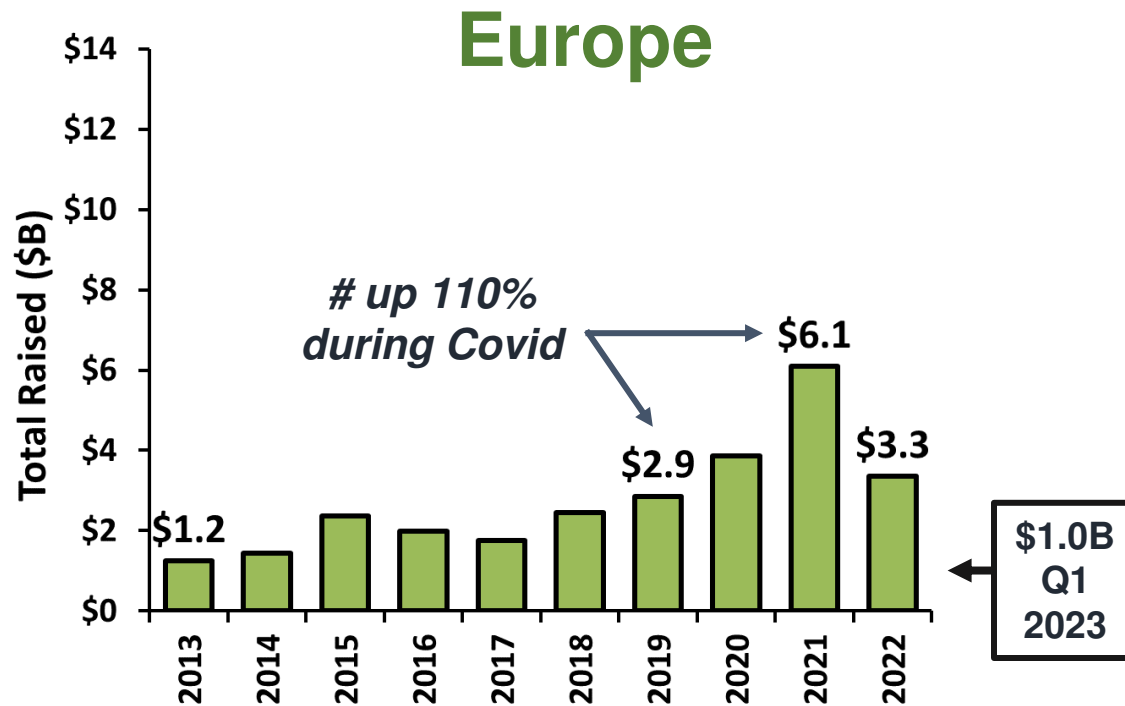
Sharp rise for Series B \$100M+ rounds in the U.S. is now reversing



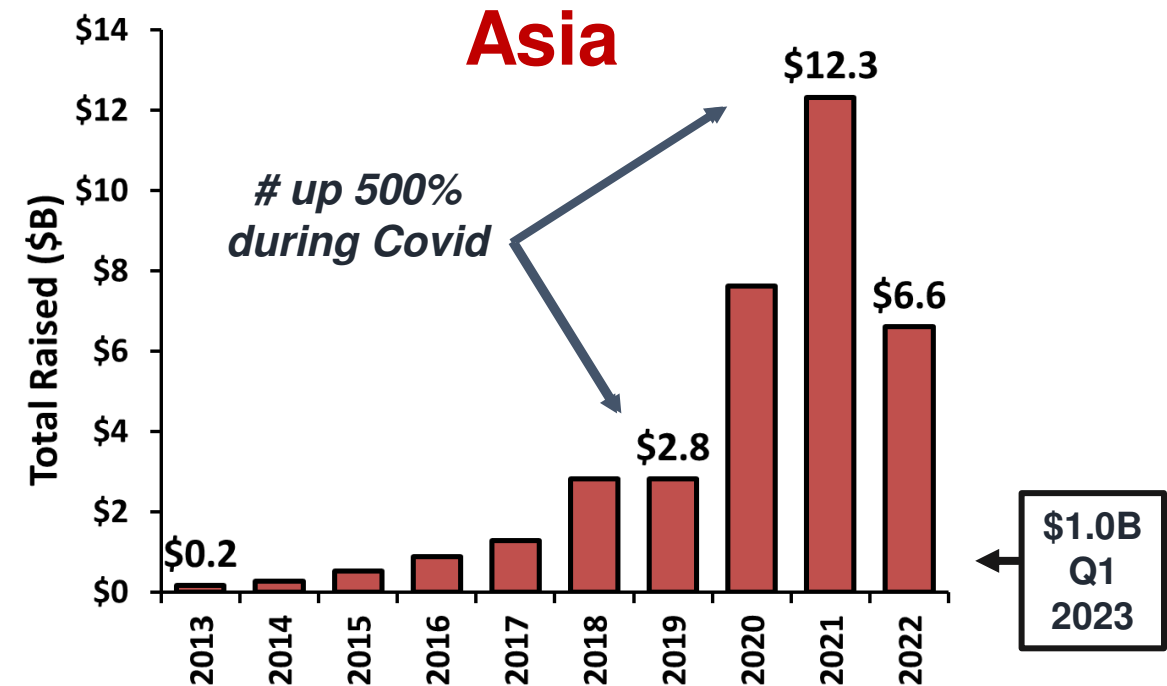
Venture Capital

Asian investment declining to European levels

2x more venture investment into Asia vs Europe for both 2021 & 2022...but not 2023 YTD



Possibly up in 2023



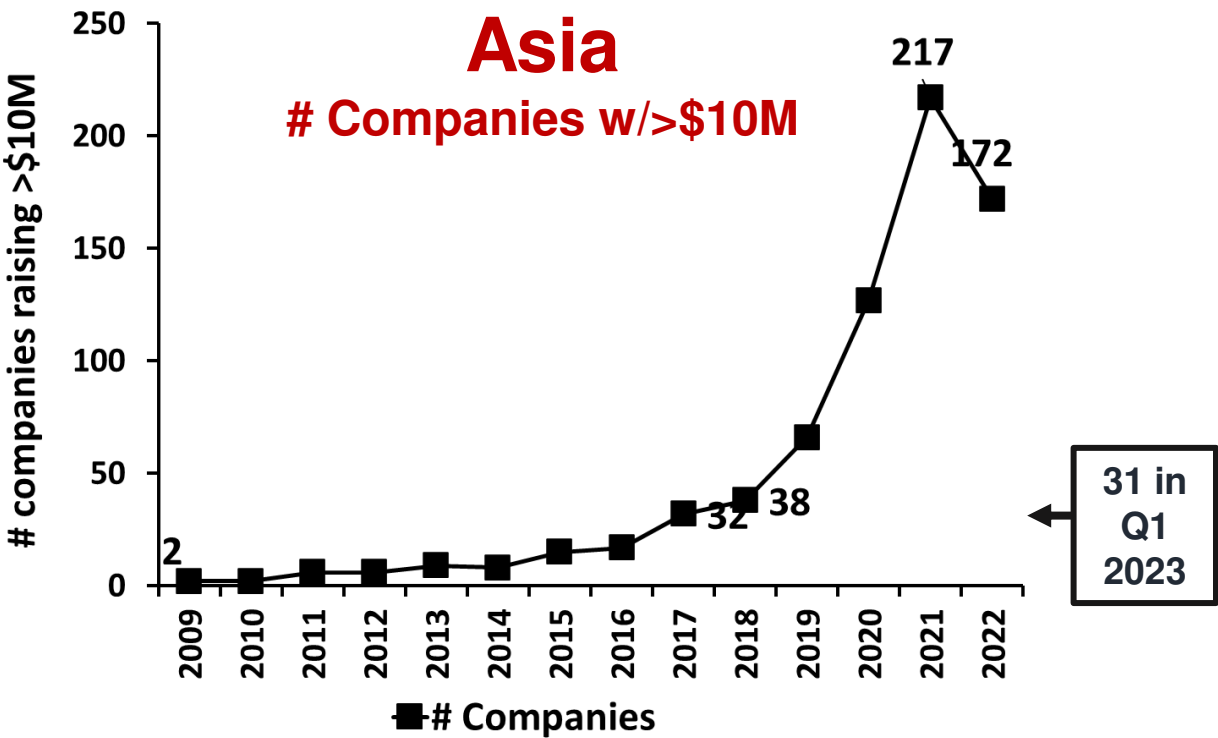
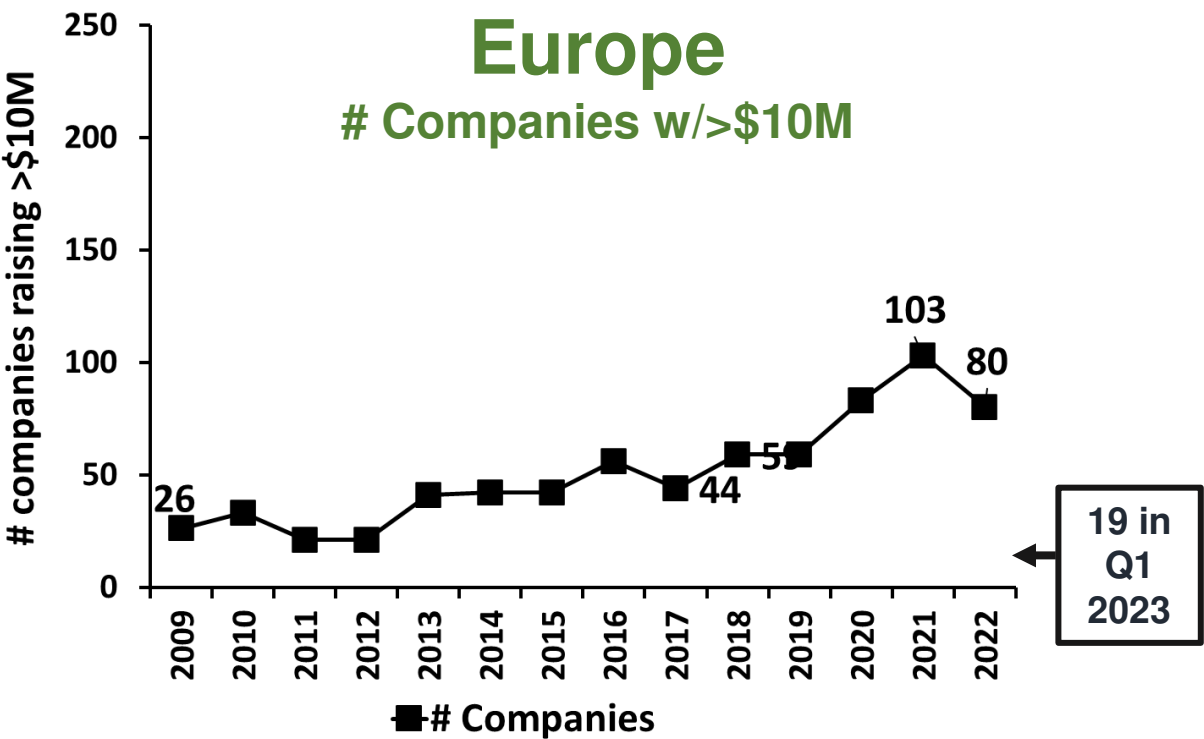
After up 1,800% in 10 yrs into 2021, declining rapidly in 2022, 2023



Venture Capital

More Biopharma companies in Asia receiving funding than Europe

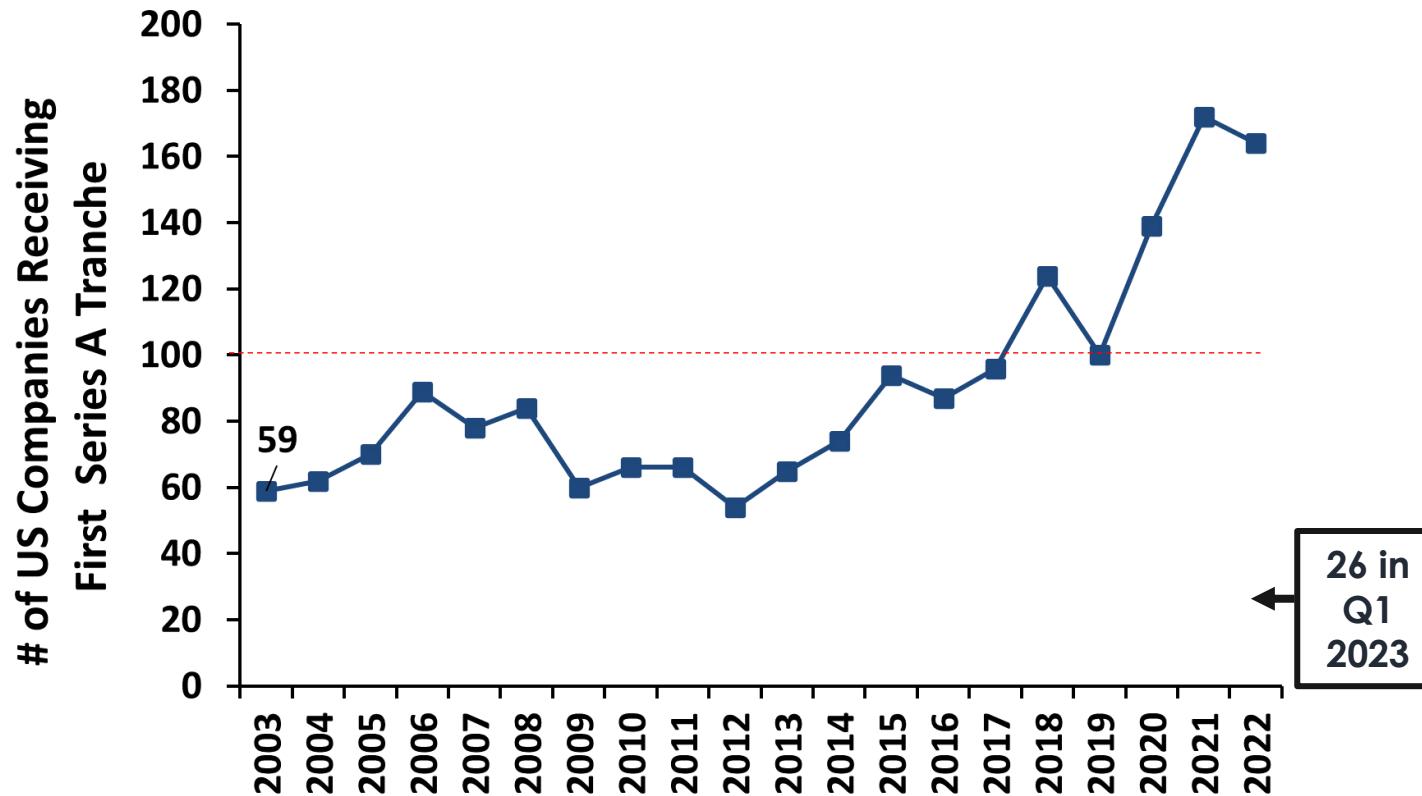
2x more companies funded with at least \$10M VC in Asia vs Europe



Venture Capital

Series A-1 rounds into U.S. Biopharma declining

Fewer A-1 rounds in 2023, with RNA-focused start-ups raising the most



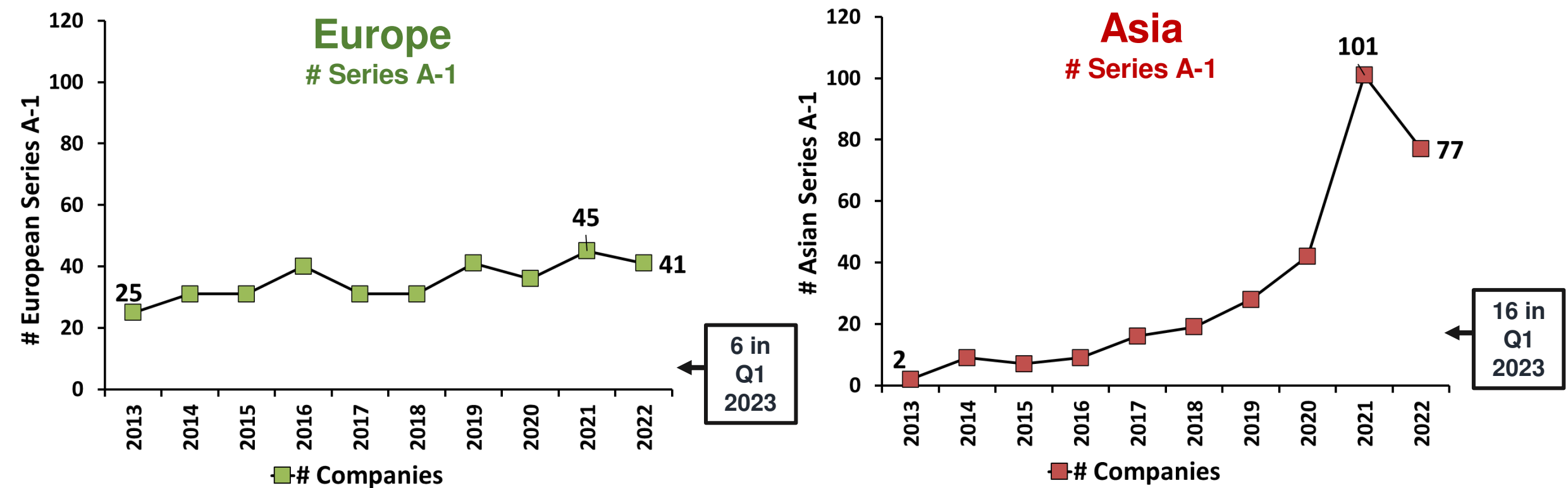
Top Series A-1 2023

- ReNAgade \$300M (PC) RNA delivery+
- Orbital, \$270M (PC) cRNA/siRNA
- Aera, \$170M A/B (PC) RNA delivery

Venture Capital

Asia has more A-1 rounds than Europe (a proxy for company formation)

Fewer A-1 rounds in 2023 likely Ex-U.S.



BIO Industry Analysis Data

www.bio.org/iareports

Daily BIO News from “Good Day BIO”

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