

## *LES 2015 Spring Meeting*

# Re-emergence of Platform Technologies -- Gonna Party Like It's 1999

May, 2015

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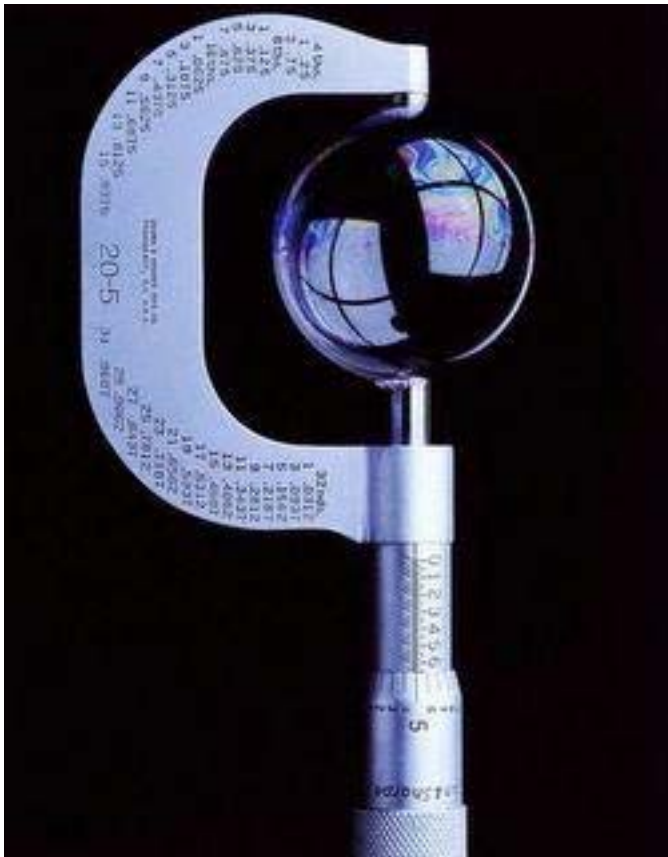
# Technology Platforms Re-emerge: Should We Be Worried?



“the market for new public [biotech] offerings has been incredibly strong over the past couple years. ...The strength of the biotech sector has led many to raise the concern of a BioBubble in valuations and sound the alarm.”

-- Forbes 3/05

# Technology Platforms Re-emerge: Should We Be Worried?



“The last downturn followed a two-year boom that started in 1998 and saw the Nasdaq Biotech Index rise fourfold. When it crashed, it took a decade for investors to get excited again.”

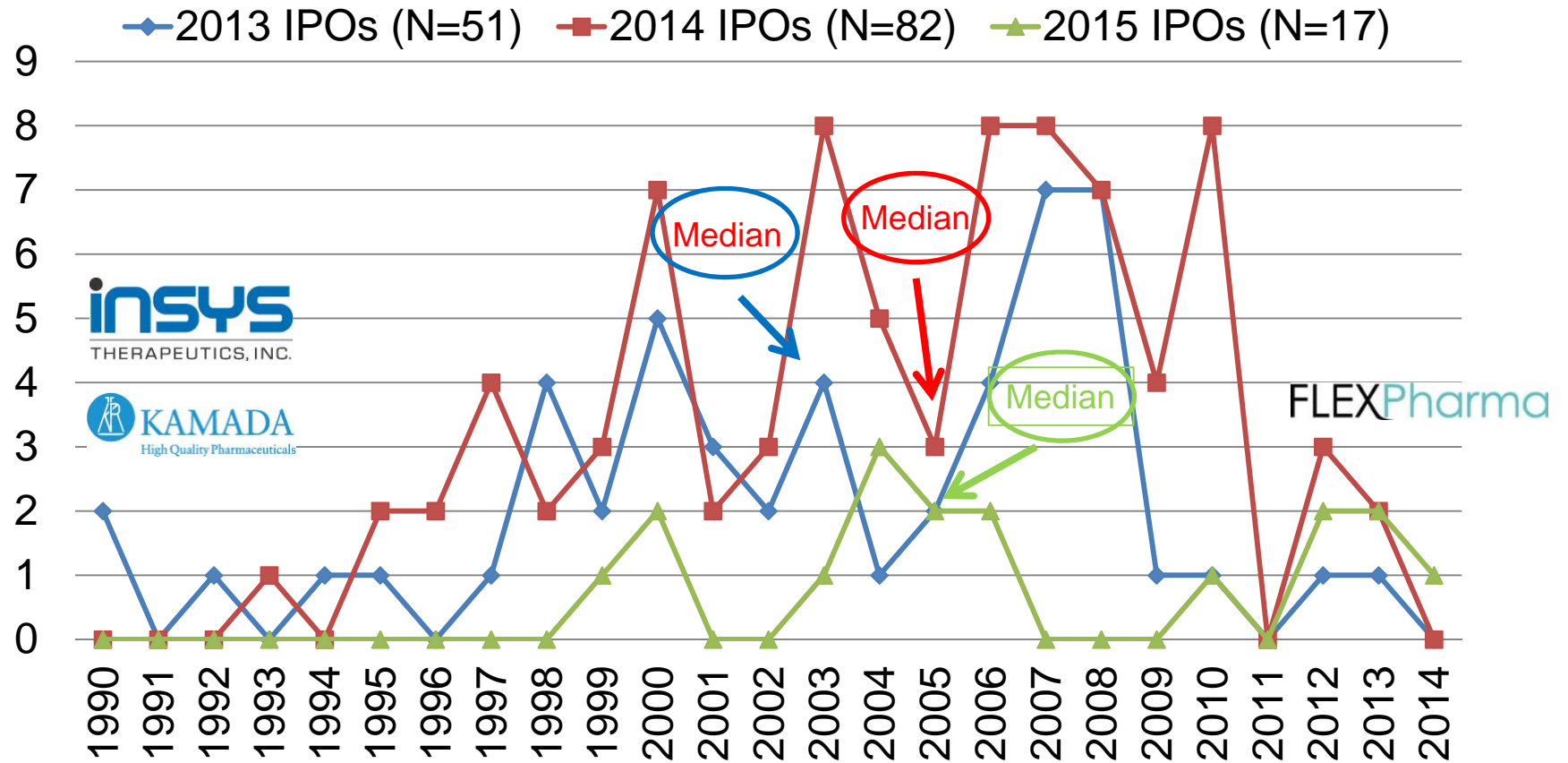
-- Bloomberg Business 3/05

# Technology Platforms Re-emerge: Should We Be Worried?

- No Argument: Biotech IPOs Generally, and Firms With Technology Platforms Specifically, Are Having Their Best Run Since the 2000 IPO Window
- Revisiting the 2000 IPO Biotechs – What Happened Then & What Followed Next?
- How Does the IPO Cohort of 2013-2015 Compare to the IPO Class of 2000?
- Are There Lessons to be Learned?

# 150 Biotechs Went Public in US

## From Jan 2013 Thru April 2015, by Founding Year



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➤ Are There Lessons to be Learned?

## “Recapping” the 2000 Biotech IPO Window



“the biotech sector is entering 2001 replete from the richest financing feast in its 25-year history. ...Biotech companies raised more money in 2000 than they had in the previous six years *combined*.”

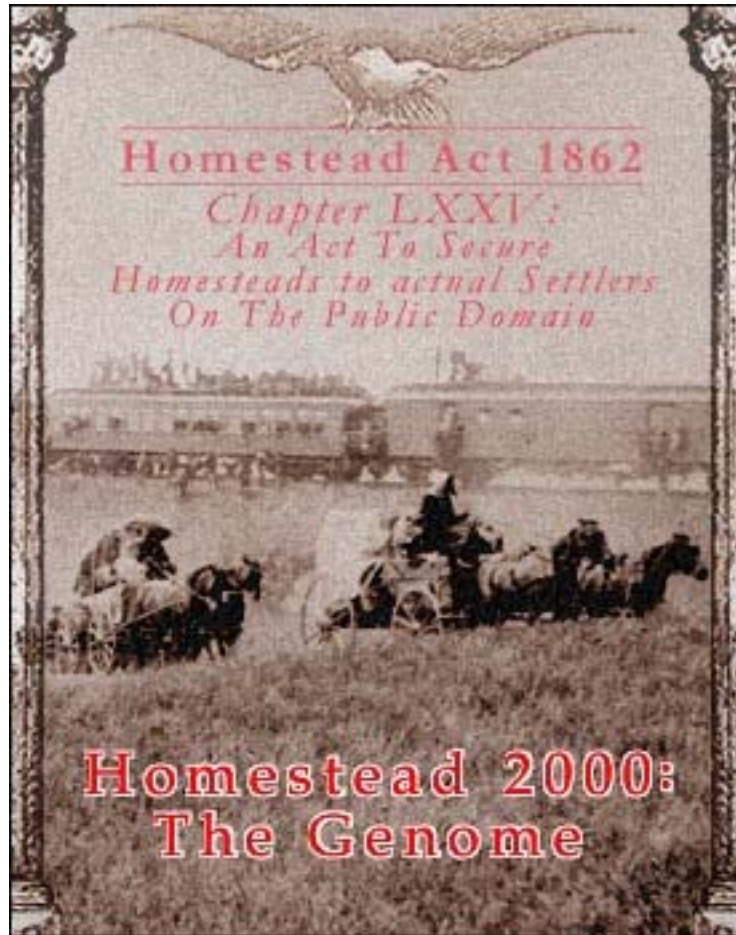
-- A Superlative Year, Signalmag.com 1/01

## “Recapping” the 2000 Biotech IPO Window

- 90 Biotech Firms Completed IPOs Between December 1999 and March 2001, 72 of These on US Exchanges, Raising \$6.8 Billion
- 57 Follow-on Offerings Were Completed in 2000, Reaping \$10.8 Billion
- All Biotech Public Offerings in 2000 Totaled \$18.5 Billion, Topping All Public Offerings in the Previous Eight Years (1992-1999) *Combined*



# Platform Technologies Dominated Financing in 2000



“the majority (almost 60 percent) [of 2000 Biotech IPOs] are platform companies rather than product companies, making their business prospects all the more difficult to ascertain.”

-- 2000 IPOs Lead the M&A Charge, Signalsmag.com 8/01

## Platform Technologies Dominated Financing in 2000

- 42 of the 2000 IPO Biotechs (58%) Were Involved in Genomics, Proteomics/SNPs, Genetics and Combinatorial Chemistry Technologies
- Only 21 of the 2000 IPO Biotechs (29%) Had Already Developed Clinical-Stage Drug Candidates as of Their IPO
- By Mid-August 2000, Biotech Genomic Stocks Were Trading, on Average, 99% Above Their IPO Prices, and More Than a Few Had Tripled in Value (vs. an Average Increase of 55% for All 2000 IPOs)

## An Embarrassment of Riches, And Choices

# TOOL TIME



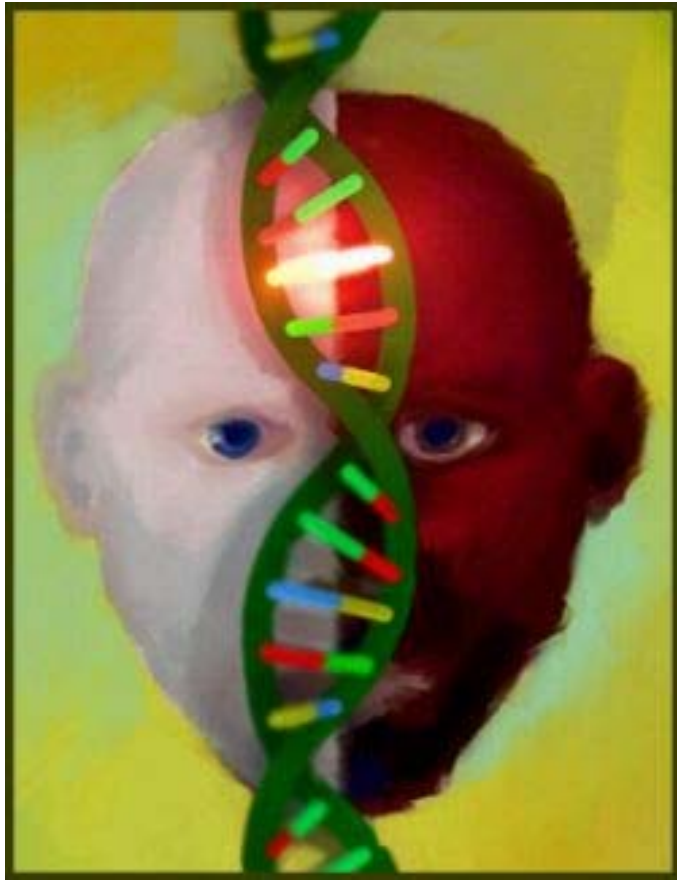
“[Biotechs] raised tremendous amounts of cash last year, more than enough to carry them forward for years to come. ...How will they now use those resources to grow their businesses?”

-- Grand Ambitions, Signalmag.com 2/01

## An Embarrassment of Riches, And Choices

- 50+ Public Biotechs had Market Caps of at Least \$1 Billion at the End of December 2000, Including Six Biotechs From the 2000 IPO Class
- 20 Biotechs Raised in Excess of \$200 Million in a Single Financing, Including Four Biotechs From the 2000 IPO Class
- Many Biotechs Had Multiple Options: Build a Manufacturing Plant, Expand Clinical Trials, Hire a Sales and Marketing Staff, or Engage in M&A

## The Financing Climate Changed Abruptly in 2001



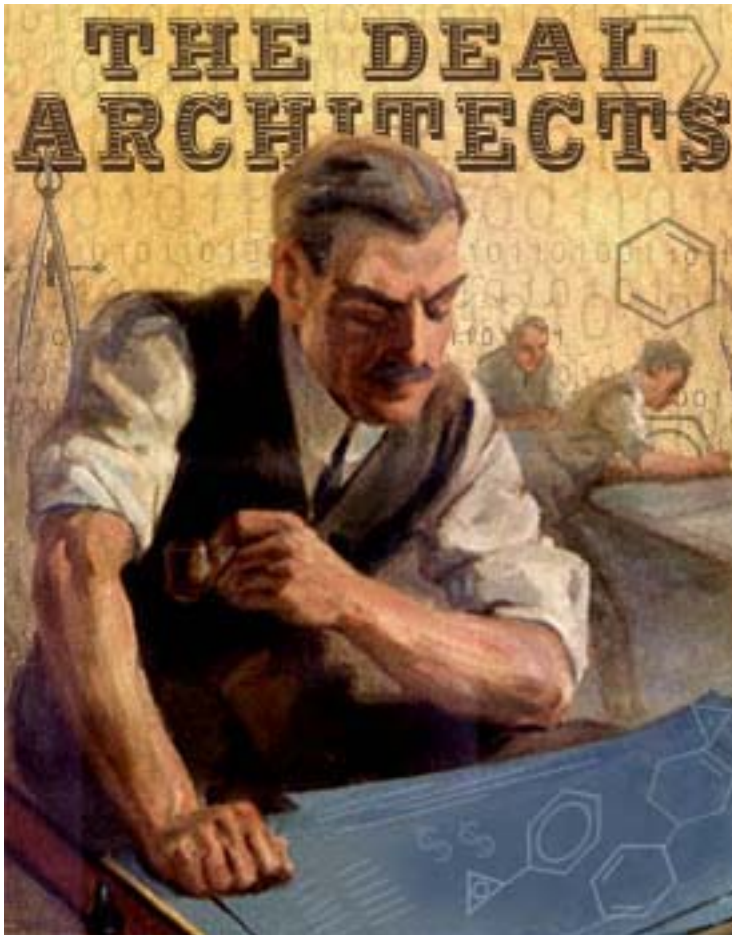
Companies built on technology platforms are “not viable as businesses” over the long term. “These companies are either going to have to acquire more like technology to enhance their share of the discovery platform or they’re going to have to become drug discovery companies themselves by adding other capabilities.”

-- Stelios Papadopoulos, SG Cowen, 8/01

## The Financing Climate Changed Abruptly in 2001

- By July 31, 2001 the Stocks of the 2000 IPO Biotechs Were Trading, on Average, 30% Below Their Closing Prices at Year-End, Underperforming the Market (Down 18%) and the NBI (Down 20%).
- By July of 2002, the Stocks of the 2000 IPO Biotechs Were Trading, on Average, 59% Below Their IPO Prices (71% Below on a Median Basis)
- Aggregate Market Cap of the 2000 IPO Biotechs Fell to 51% of IPO Valuations, from \$25.9 Billion to \$13.1 Billion in July 2002

## What Happened Next? IPO Class Goes Separate Ways



“We’re keeping the end-game in mind: First the targets, then the drugs. I don’t believe there is a successful strategy other than working towards our own products. There are a number of companies with a variety of business models, but there is only one successful model.”

-- George Scangos, CEO of Exelixis 8/01

## What Happened Next? IPO Class Goes Separate Ways

- Of the 42 Platform Biotechs that Went IPO in 2000, Almost Half Were Involved in M&A in 2001:
  - 15 Genomic/Tools Acquisitions & 2 Sales
  - 2 Drug Discovery Acquisitions & 1 Sale
  - 2 Clinical-Stage Acquisitions
- In 2001, Biotechs Formed 1,100+ New Alliances, 442 with Big Pharma & 745 with Other Biotechs
- In 2002, 58 US Biotechs Initiated Restructuring Moves to Conserve Cash; 37 Publicly Traded Biotechs Received Warnings or Delisting Notices; 8 Public Biotechs Filed for Bankruptcy or Liquidation



## Where Are They Now? 2000 IPO Biotech Outcomes

- 35 Biotechs Were Acquired:
  - 8 with 1.0+ Multiples on IPO Mkt Cap & IPO \$/share
  - 4 with 1.0+ Multiple on IPO Mkt Cap only
  - 23 with <1.0 Multiples on IPO Mkt Cap
  
- 29 Are Free-standing Biotechs:
  - 11 with Current Market Capitalizations > \$1 Billion
  - 8 with Current Market Capitalizations > IPO Mkt Cap
  - 10 with Current Market Capitalizations < IPO Mkt Cap
  
- 8 Became Bankruptcies & Liquidations

# Best Outcomes of 2000 IPO Biotechs

## Clinical Compounds & Diagnostics

• InterMune (19.2x) (Compounds)	• \$8,300M (8/14) (Acq by Roche)
• Versicor (Vicuron) (7.6x) (Compounds)	• \$1,900M (6/05) (Acq by Pfizer)
• Esperion (5.9x) (Compounds)	• \$1,300M (12/03) (Acq by Pfizer)
• Crucell (4.4x) (Compounds)	• \$2,400M (10/10) (Acq by J&J)
• Ista Pharmaceuticals (3.4x) (Compounds)	• \$500M (3/12) (Acq by Bausch)
• IntraBiotics (Ardea) (3.0x) (Compounds)	• \$1,260M (4/12) (Acq by AstraZeneca)
• Inspire (1.4x) (Compounds)	• \$430M (4/11) (Acq by Merck)
• Adolor (1.0x) (Compounds)	• \$415M (10/11) (Acq by Cubist)
• Seattle Gen (21.4x) \$4.3B (Compounds)	• Exact Sci (8.9x) \$2.2B (Diagnostics)
• Charles River (5.9x) \$3.4B (Reagents)	• Medicines (3.6x) \$1.8B (Compounds)

## Technology Platforms

• Tularik (2.1x) (Genomic Targets)	• \$1,300M (3/04) (Acq by Amgen)
• Rosetta Inpharmatics (1.4x) (Genomic Targets)	• \$620M (5/01) (Acq by Merck)
• Third Wave (1.4x) (Bioinformatics)	• \$591M (6/08) (Acq by Hologics)
• Packard Bioscience (1.2x) (Genomic Equipment)	• \$650M (7/01) (Acq by Perkin Elmer)
• App Molecular (0.9x) (Genomic Targets)	• \$400M (11/03) (Acq by Lilly)
• Illumina (53.3x) \$27.3B (Genomic Equipment)	• Keryx (5.7x) \$1.1B (Bioinformatics)
• Cepheid (26.0x) \$4.1B (Genomic Equipment)	• Arena (2.5x) \$1.0B (Genomic Targets)
• Dyax (13.0x) \$3.6B (Combi Chemistry)	• Array (5.9x) \$1.0B (Combi Chemistry)
• Bruker (4.7x) \$3.3B (Genomic Equipment)	

## “When They’re Passing Out Hors d’oeuvres ...”

- 1999 to 2003 Alliances by Top Third 2000 IPO Biotechs
  - 200+ Alliances Over a Four Year Period
  - 23 Key Alliances (\$25M+ in Pre-Launch Payments)
- Key Alliances Provided Sustainability & Momentum
  - \$2 Billion in Aggregate Payments (\$82M Average)
  - 8.3% Average Effective Royalty Rate (on \$500M)
  - Three Deals with 50/50 Profit Split Potential
- One (Tularik/Amgen) Led to Acquisition at a Premium

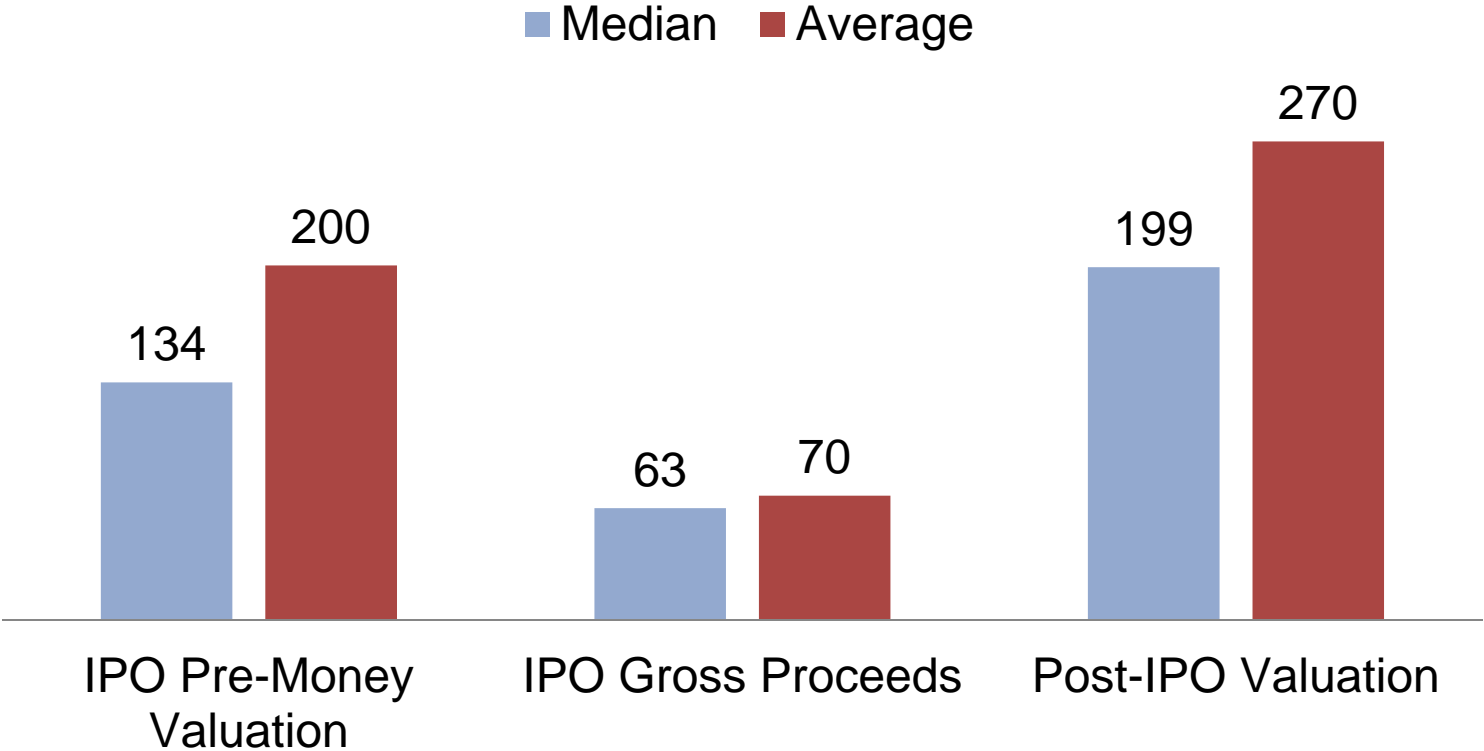
## The Other End of the Spectrum – Worst 2000 IPO Biotech Outcomes

- 8 Bankruptcies & Liquidations:
  - 3 Genomic Platforms (2 Proteomics/SNPs, 1 Targets)
  - 1 Bioinformatics & 1 Combi Chemistry Platform
  - 3 Clinical Compounds (2 in 2008 & 1 in 2014)
  
- 16 Firesale Acquisitions (Exit < 50% of IPO Mkt Cap):
  - 6 Genomic Platforms (3 Proteomics/SNPs, 1 Targets, 2 Equipment)
  - 3 Bioinformatics & 3 Combi Chemistry Platforms
  - 4 Clinical Compounds (1 in 2002, 2 in '05 & 1 in '06)

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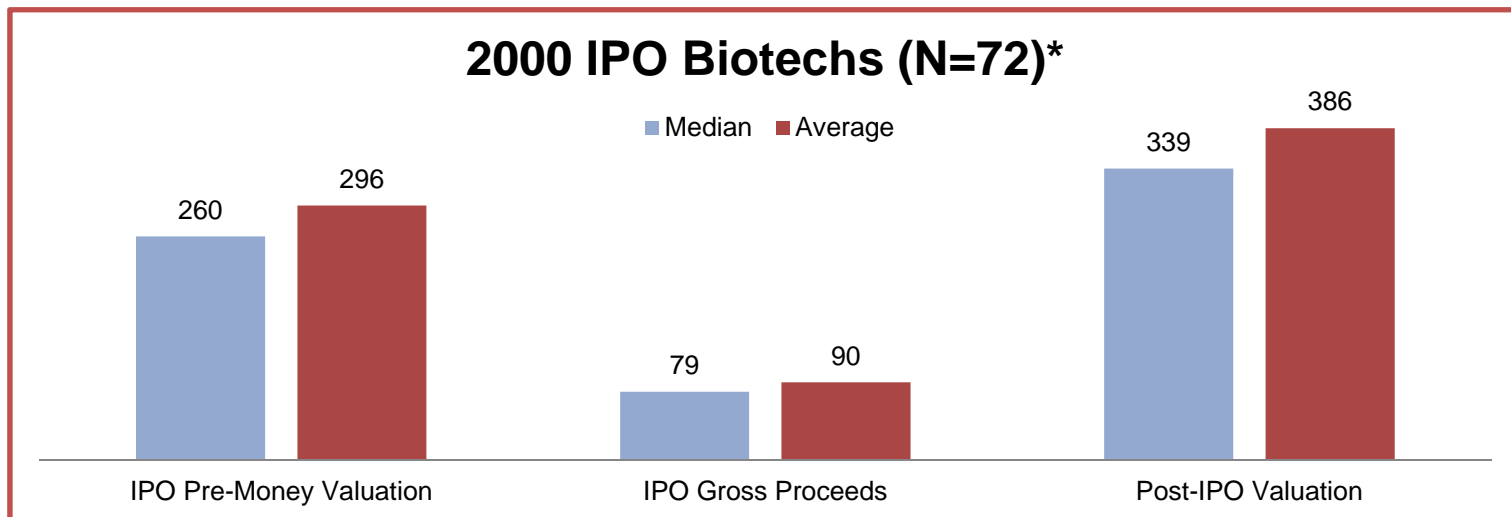
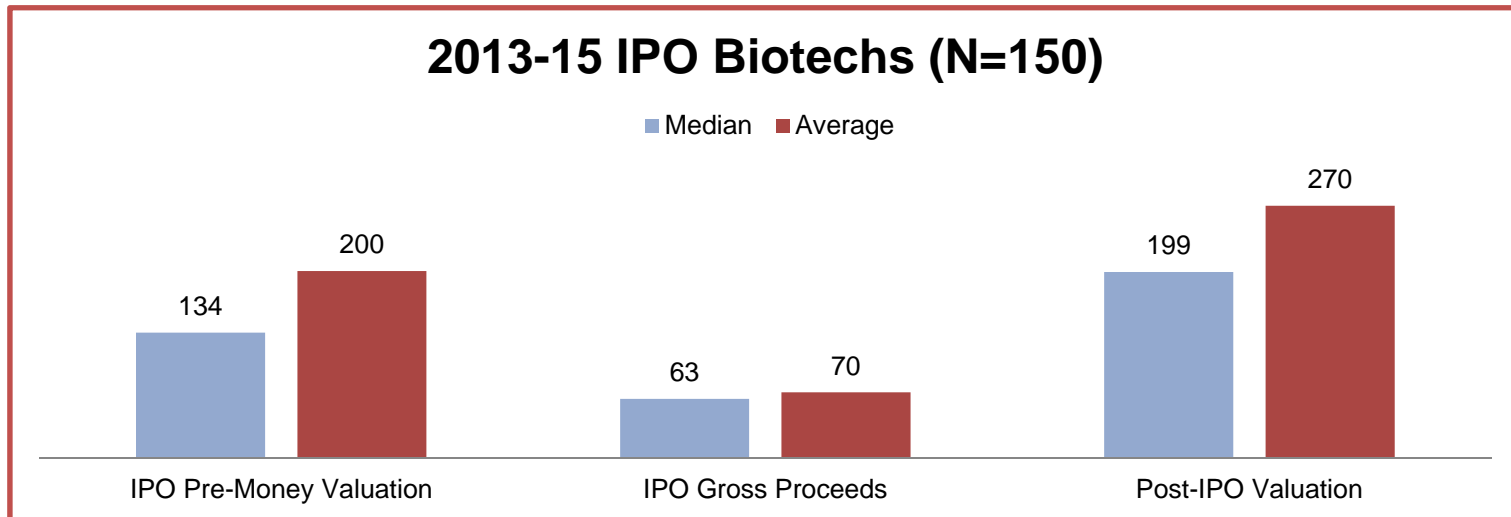
# 2013-2015 Biotech IPO Class: Valuation at IPO (\$M)\*



\* 150 US Biotech IPOs, \$10.5B in Aggregate IPO Gross Proceeds

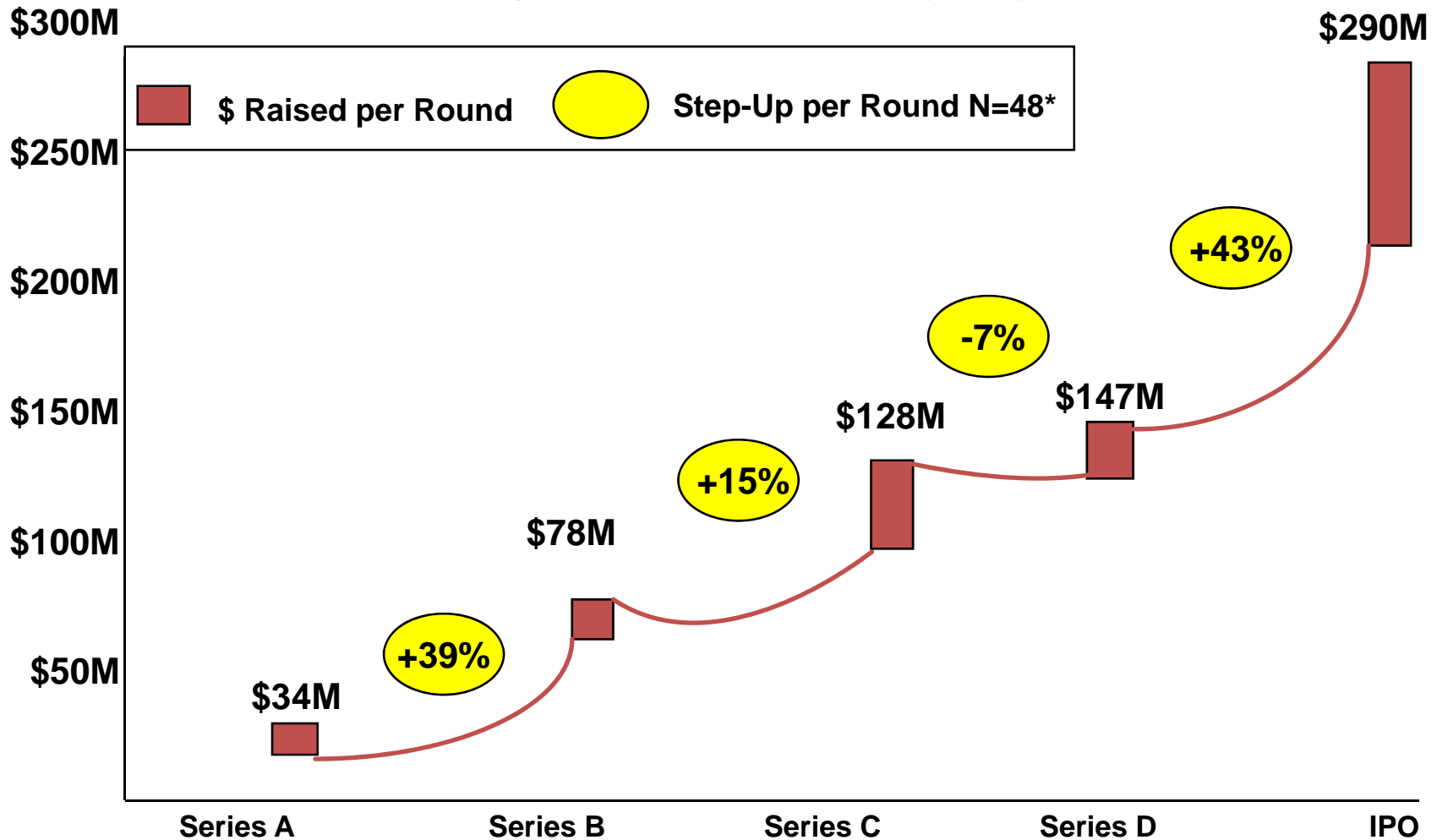


# 2013-15 IPO Biotechs Vs. 2000 IPO Biotechs



\* 72 US Biotech IPOs, \$6.8B in Aggregate IPO Gross Proceeds

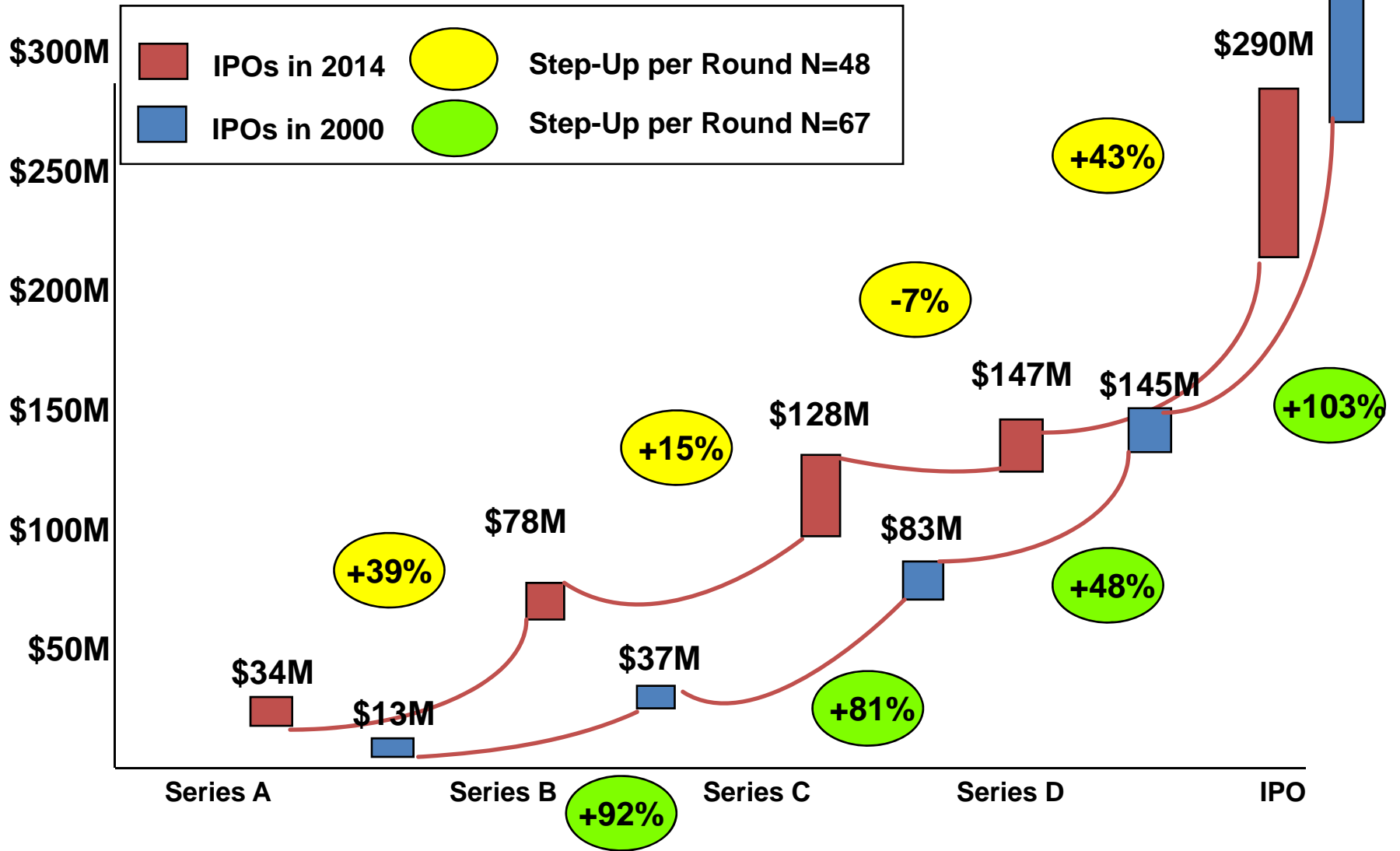
# 2014 VC-Backed Biotech IPOs: Average Valuation Step-Ups



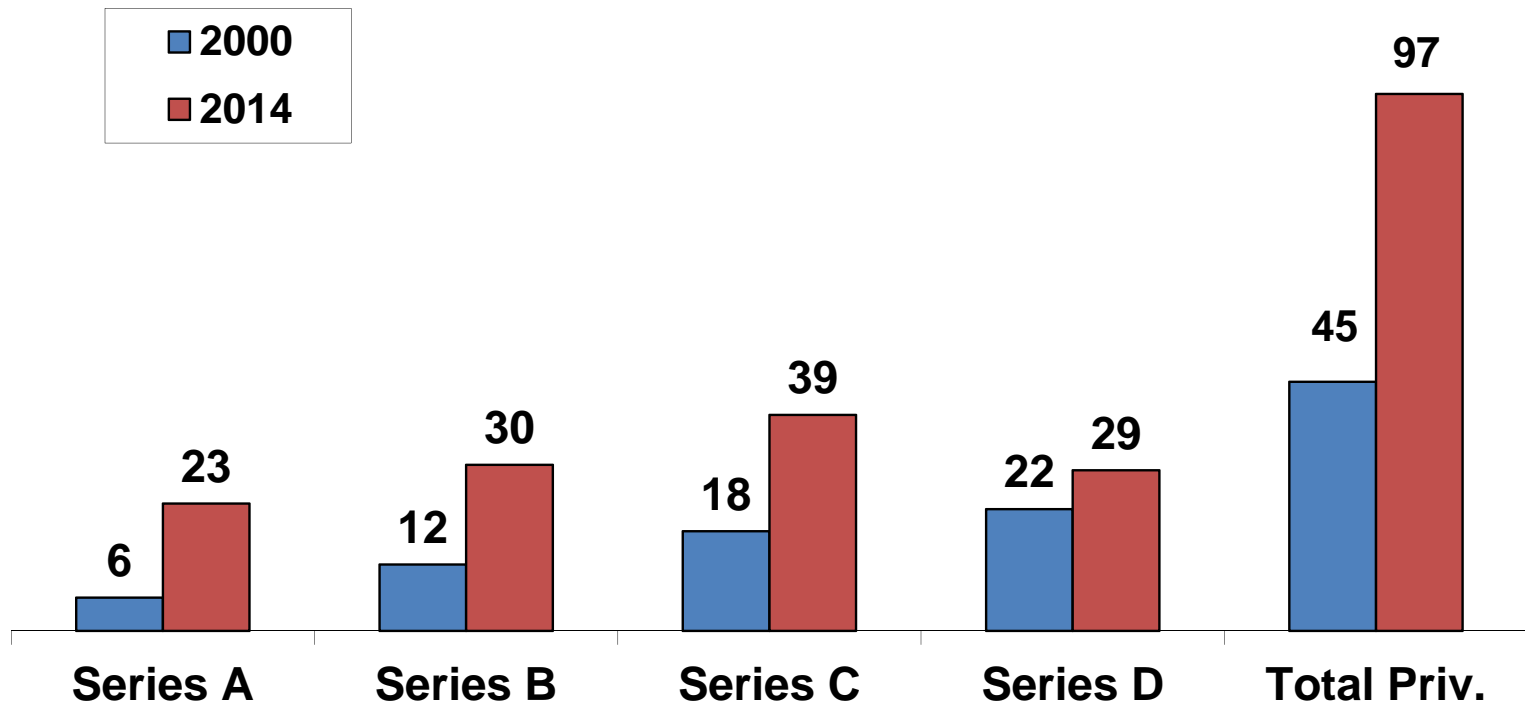
\* 82 Biotechs completed IPOs in 2014; excludes 14 not VC-backed & 20 recapitalized or with 6+ private financings



# 2014 Biotech IPOs Vs. Biotech IPOs of 2000



# Average Private Round Financings of 2014 Vs 2000 VC-Backed Biotech IPOs



## How Does the Current IPO Cohort Compare to 2000?

- 42 (58%) of the 2000 IPO Biotechs Were Platforms in Genomics, Proteomics/SNPs, Genetics and Combinatorial Chemistry Technologies
  
- 61 (41%) of the 150 Biotechs That Went Public on US Exchanges from January 2013 Thru April 2015 Claimed Proprietary Technology Platforms in Their Prospectuses; Platforms by Calendar Year of IPO:
  - 22 (43%) of 2013 IPO Biotechs
  - 33 (40%) of 2014 IPO Biotechs
  - 6 (35%) of 2015 IPO Biotechs YTD

## What Are the Platforms of the 2013-15 IPO Biotechs?

➤ Technology Platforms of the Current IPO Cohort Are Broadly Grouped as Follows:

- Small Molecule Discovery & Design
- Approaches to Genetic & Orphan Diseases
- Protein, Antibody & Vaccine Discovery & Design
- Immunotherapy, Cell & Gene Therapy

➤ Whereas No Platforms and Only 29% of All 2000 IPO Biotechs Were in the Clinic, 54 (89%) of the Current IPO Cohort With Platforms Are in Clinicals

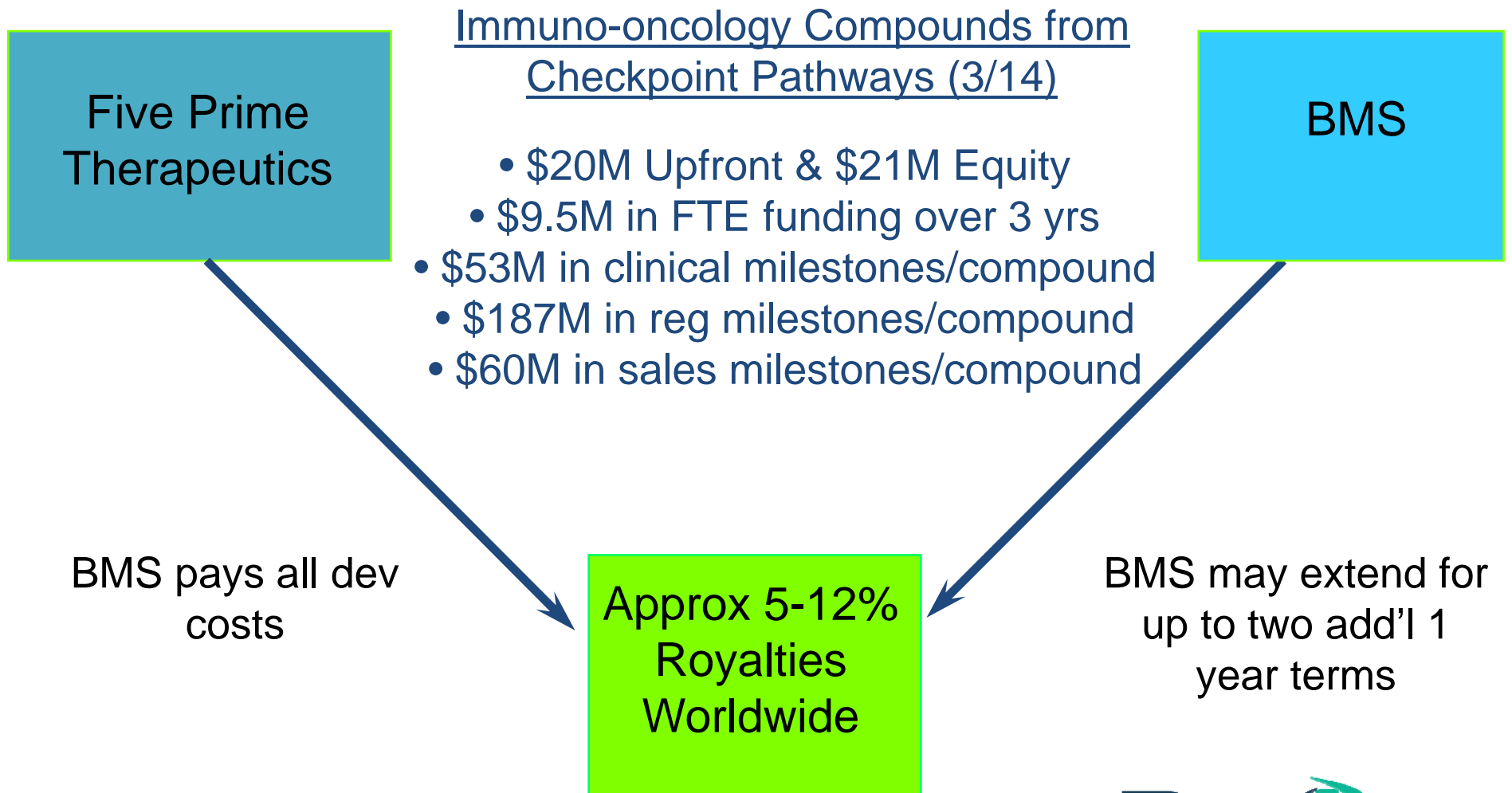
## Which Platforms Are “Trending” Most Recently?

- Small Molecule Discovery & Design:
  - 7 IPOs in 2013, 9 IPOs in 2014, 0 YTD
- Approaches to Genetic & Orphan Disease:
  - 4 IPOs in 2013, 4 IPOs in 2014, 0 YTD
- Protein, Antibody & Vaccine Discovery & Design
  - 6 IPOs in 2013, 3 IPOs in 2014, 2 YTD
- Immunotherapy, Cell & Gene Therapy
  - 5 IPOs in 2013, 17 IPOs in 2014, 4 YTD

## “When They’re Passing Out Hors d’oeuvres ... Revisited”

- 2012 to 2015 Alliances by the Current IPO Cohort
  - There Have Been 41 “SEC-Filed” Alliances Signed Since January of 2012 With Total Announced Payments to the Licensor of at Least \$400 Million
  - 23 (56%) of These “Big Ticket” Recent Alliances Have Involved the Current IPO Cohort
- \$22.4 Billion in Potential Payments From Recent IPO Cohort Alliances (\$935M Average Per Alliance)
- Already There Have Been Three Post-IPO Acquisitions (Omthera, Ambit, Prosensa)

# Discovery & Pre-clinical Development Alliance: Three Year Research Collaboration



# Discovery & Early Clinical Stage Alliance: Developing a Platform for a Therapeutic Franchise

## AVA-101\* anti-VEGF & 8 Proteins Via Gene Therapy for Ophthalmic Uses (5/14)

- \$2M upfront, \$5M equity plus \$10M add'l equity at IPO
  - \$80M in R&D reimb per product for AVA-311 and 7 add'l therapeutic proteins over 3 yr research term
  - REGN initially evaluating AVA-311 in preclinical studies for treatment of juvenile X-linked retinoschisis (XLRS)
  - Low- to Mid- single-digit royalties

Avalanche

Regeneron

Avalanche has option of 10-35% co-dev & profit share for up to 2 of 8 therapeutic targets

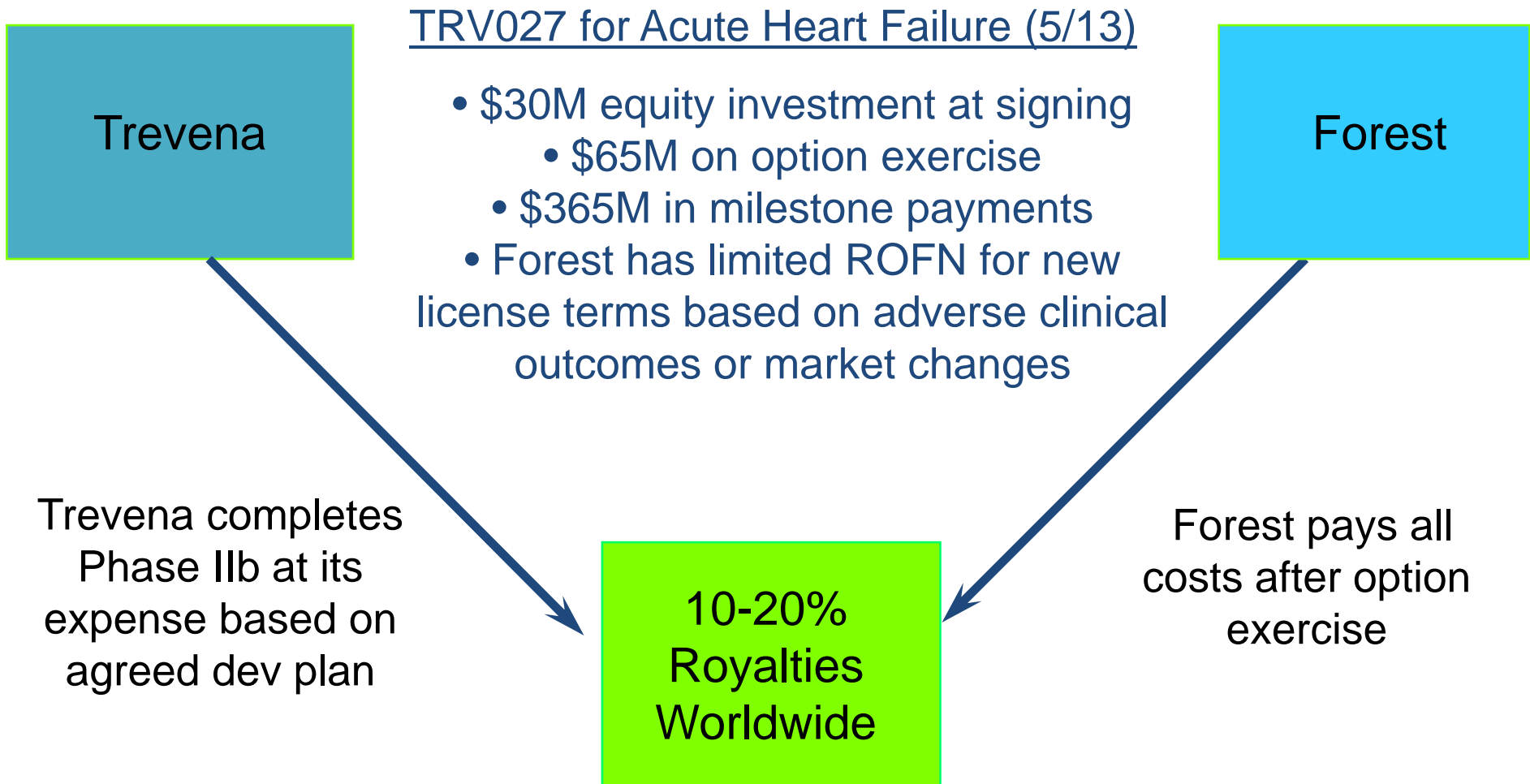
Low- to Mid-  
Single Digit  
Royalties

REGN has option to exclusive ww license for each product after IND filing;  
REGN has ROFN to AVA-101

\* AVA-101 (anti-VEGF for wet AMD) is most advanced, with Ph 2a data expected in mid-2015

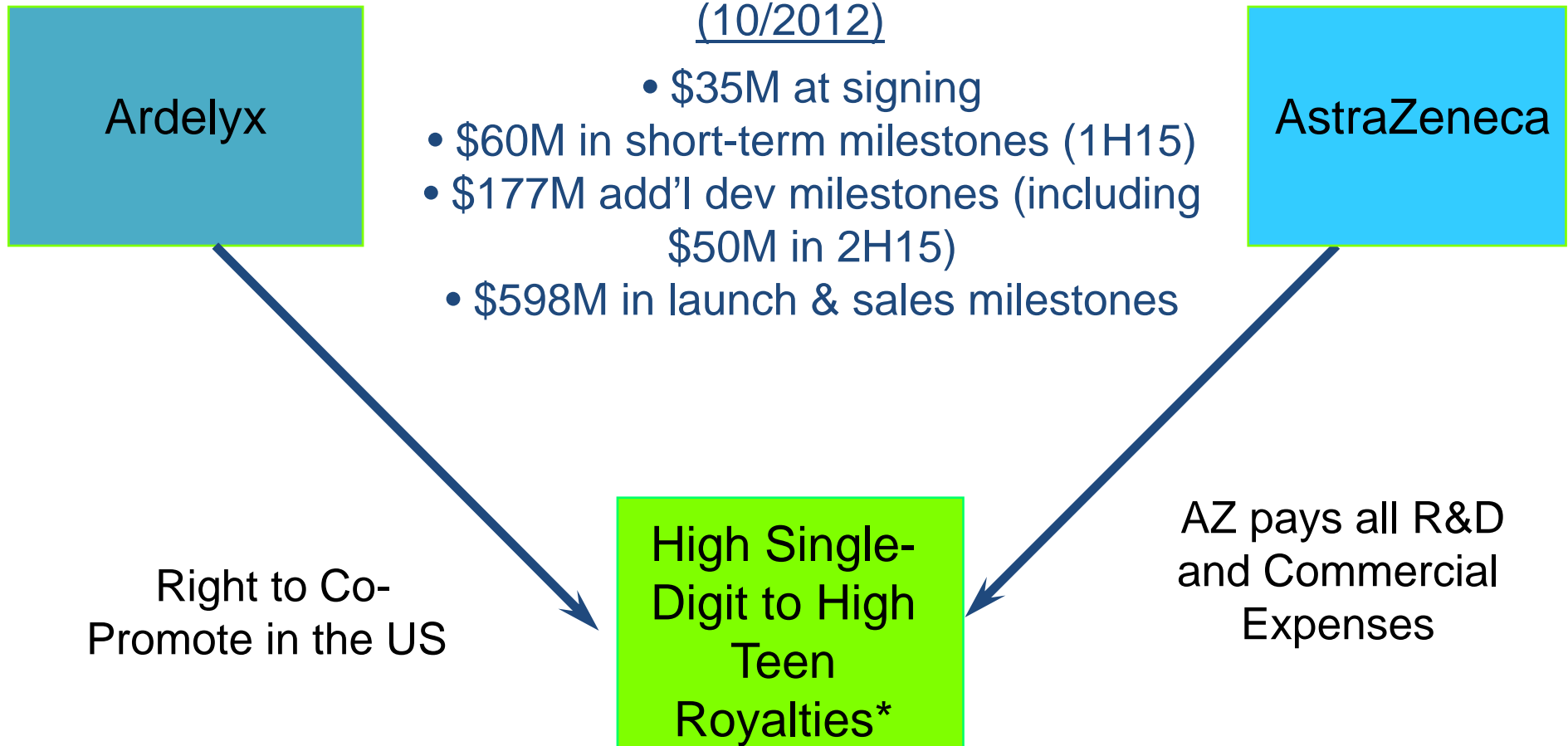


# Option on a Phase II Compound: Payment for a “No-Shop” Period and Pre-Set Terms



# License to a Phase 2a Compound: Stepping Lightly into the Co-Development Pond

## Tenapanor (NH3 Inhibitor) for Renal Diseases (10/2012)



\* Ardelyx has Co-Fund Option at end of Ph II -- \$20M, \$30M or \$40M for 1%, 2% or 3% add'l Royalty

# Phase II Compound License & Option to 10 Biologics: Cancer Stem Cell (CSC) Alliance Around 3 Signaling Pathways

Demcizumab, DLL4/VEGF bispecific Mab,  
plus 4 biologics to RSPO-LGR & One Add'l  
Signaling Pathway (12/13)

OncoMed

Celgene

- \$155M Upfront Payment & \$22M Equity
- \$790M in milestones for Demcizumab
  - \$505M in milestones for bispecific
  - \$440M/compound in option & dev milestones for 4 add'l biologics
- \$100M if Celgene elects to extend rights to small molecules

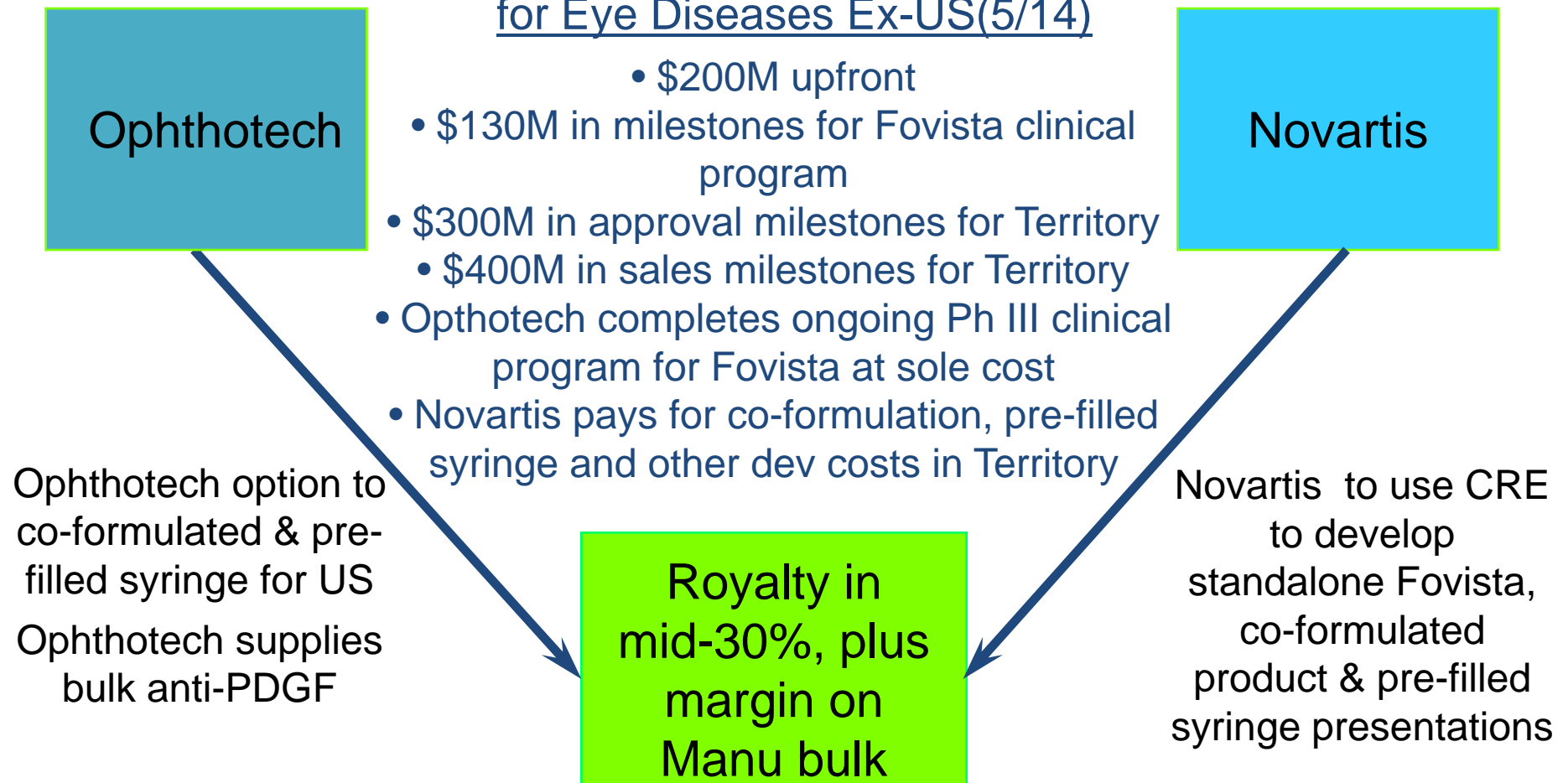
OncoMed pays thru Phase II on first and Phase I on each add'l biologic (up to 6); option to co-dev in US if pay 1/3 of global dev costs

50% Profits in US & Approx 7-15% Royalty in ROW

Celgene has 4 yrs to designate specific compounds in each pathway & pays all dev costs after option (subject to co-dev option)

# Phase III Compound Deal for Ex-US Rights: Integrating a New Compound into a Successful Franchise

## Fovista (Anti-PDGF Aptamer) & Anti-VEGF Co-formulation for Eye Diseases Ex-US(5/14)



\* Anti-VEGF Co-formulation is Fovista with Lucentis or another Anti-VEGF compound

# ROW Rights to a Phase III Ready Compound: Combining US & China Rights to Accelerate Commercialization

## Roxadustat (FG-4592 Oral HIF Inhibitor) for Anemia in US, China & ROW\* (7/13)

FibroGen

AstraZeneca

- \$220M at signing
- \$192M in non-contingent funding
- Co-dev funding ex-China capped at \$116.5M (< 50% CKD dev costs)
  - \$571M in clinical & regulatory milestone payments
  - \$653M in sales milestones

50/50 sharing of costs  
& profits in China

AZ pays all comm'l  
costs ex-China

Low- to Mid-  
20% Royalty &  
Transfer Pice

\* FibroGen partnered Japan rights in 10/04 & European rights in 4/06, both to Astellas, for \$360M upfront and \$618M add'l payments



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## Technology Platforms Re-emerge: Lessons Learned

- Buying is Easy, Being Bought is Much Tougher
- Platform & Clinicals > Platform or Clinicals Alone
- Biotech is Like Long Distance Cycling – It's an Endurance Event & the Steep Slopes Are Treacherous, Both Going Up and Coming Down
- Better to Compete for Partners Than for Capital
- Structure Alliances As If Your Future Depends on Them ... It May

... and BioSciDB Shows You Best Practices, Then & Now

The screenshot shows a web browser window displaying the BioSciDB interface. The left sidebar contains navigation options: DASHBOARD, SEARCH, BROWSE, CONTRIBUTE, APPROVE, and DEV. The main content area is titled "Research & Development / Benchmark Amounts" and "Sales-based milestones". It features a paragraph of text under the heading "7.2.2 Net Sales Milestones" and a table with two columns: "Annual Calendar Year Net Sales for Products in the Territory in all Indications" and "Payment". The table lists seven sales thresholds and their corresponding payment amounts, with the text highlighted in yellow. The browser's address bar shows the URL "https://www.biosciadb.com/tag/gettag/7fed0eca-f26f-411c-b0a2-0661675ecf0c".

**7.2.2 Net Sales Milestones.** Takeda shall pay, in accordance with Section 7.4, to Orexigen the applicable Net Sales threshold milestone payments set forth in the table in this Section 7.2.2, below, the first and only the first time during the Term that the total aggregate Net Sales of all Products (including all Indications and formulations of such Products) in any Calendar Year by Takeda, its Affiliates and its Sublicensees in the Territory reach or exceed the relevant amounts set forth in the table in this Section 7.2.2, below.

Annual Calendar Year Net Sales for Products in the Territory in all Indications	Payment
Net Sales in one Calendar Year are greater than \$400 million	\$40 million
Net Sales in one Calendar Year are greater than \$600 million	\$60 million
Net Sales in one Calendar Year are greater than \$800 million	\$80 million
Net Sales in one Calendar Year are greater than \$1 billion	\$100 million
Net Sales in one Calendar Year are greater than \$1.5 billion	\$150 million
Net Sales in one Calendar Year are greater than \$2 billion	\$200 million
Net Sales in one Calendar Year are greater than \$2.5 billion	\$250 million





# See for Yourself with Our Two Week Free Trial

The screenshot shows the BioSciDB website homepage. At the top, the browser address bar displays 'https://www.bioscidb.com'. The website header features the BioSciDB logo and navigation links for 'FEATURES', 'PRICING', 'CONTACT', 'LOG IN', and 'REGISTER'. The main content area includes a large heading 'Welcome to the BioSciDB Network' and a sub-headline: 'The most comprehensive peer-reviewed reference database on biopharma alliances, sponsored by the founders who brought you Recap.com, the gold standard in tracking and analyzing biopharma alliances for two decades.' Below this is a green button labeled 'SEE HOW IT WORKS'. To the right, a laptop displays a search interface for 'Alliance Keywords' with various filters and a search button. At the bottom of the main section, there are two buttons: 'SIGN UP NOW' and 'REQUEST A FREE TRIAL', separated by the word 'OR'. Below this is a section titled 'Unparalleled Personal Benefits' with three placeholder icons. The browser's taskbar at the bottom shows two open tabs: 'View Tag: BioSci.DB.html' and 'Sales\_Milestone\_Ex.html', along with a 'Show all downloads...' button.



Thanks for Attending,  
& I hope to See You at the LES Annual Meeting

