

The BioPharma Industry in 2015: As Good as it Gets



Mark G. Edwards
Managing Director



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- How big have Biopharma Alliances gotten? Let's start with 300+ deals with at least \$50M in payments ...
 - Announced Deal Size of 2012-15 Alliances
 - Alliances as Compared to Other Deal Activity
 - Components of 2012-15 Alliance Payments
- Effective Royalty Rates in Biopharma Alliances
- “Recapping” the Biotech IPO Window
- What's Hot & What's Next

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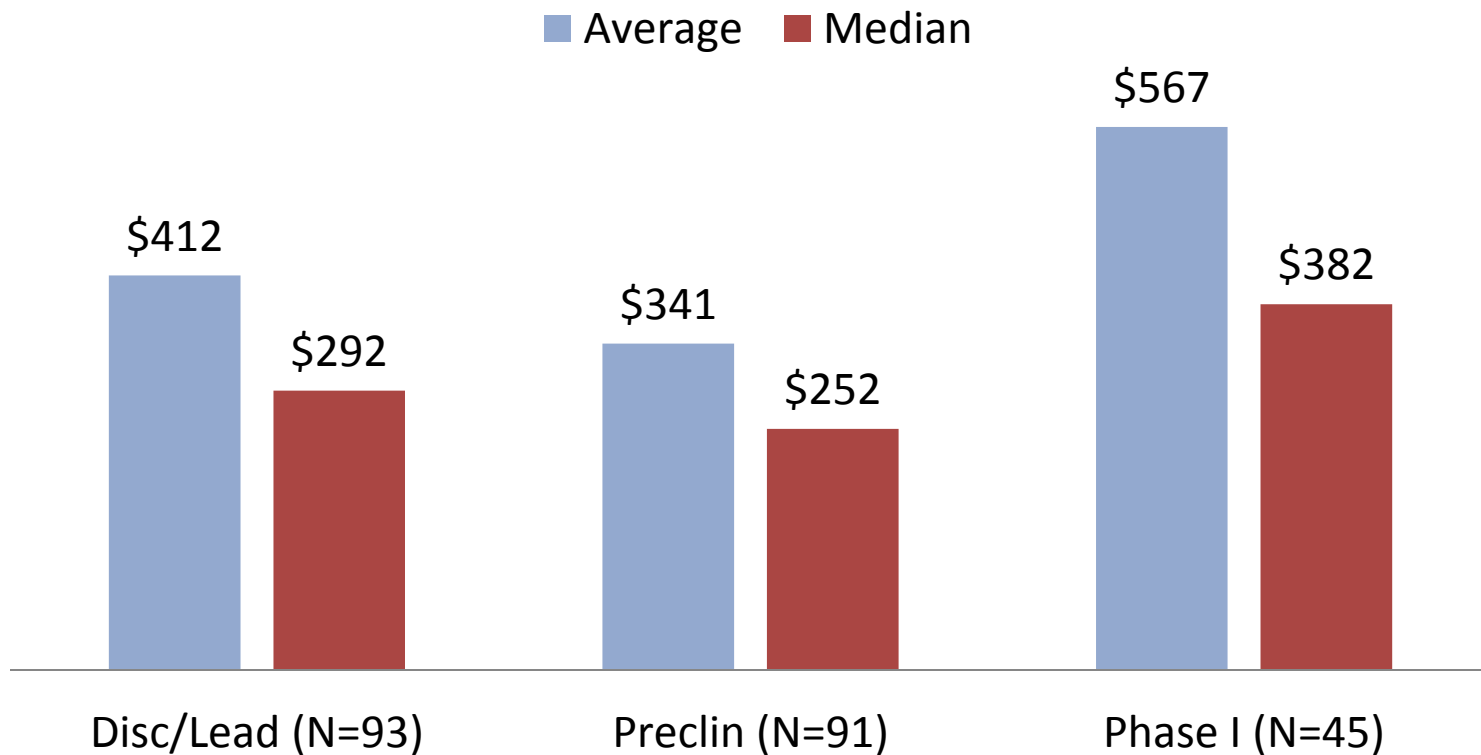
➤ Components of 2012-15 Alliance Payments

➤ Effective Royalty Rates in Biopharma Alliances

➤ “Recapping” the Biotech IPO Window

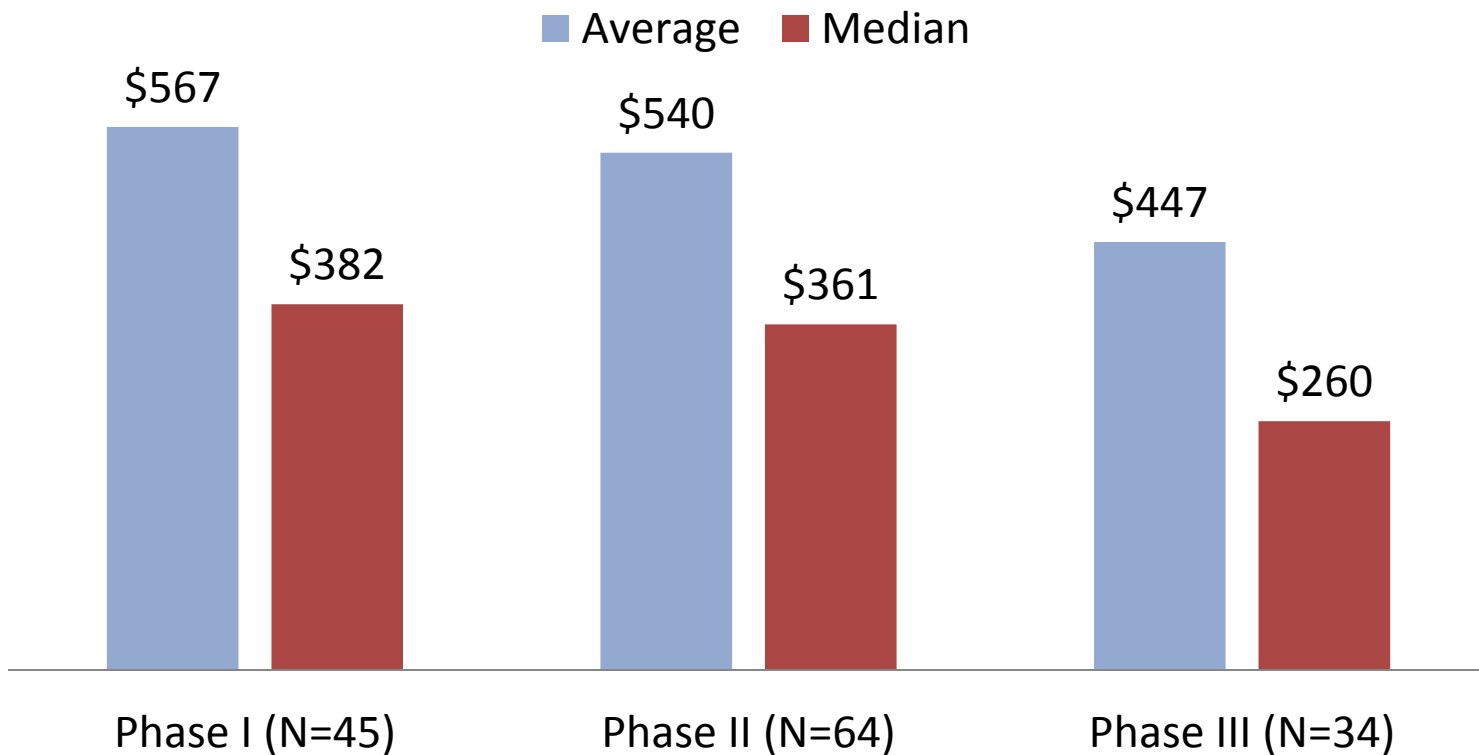
➤ What's Hot & What's Next

Announced Deal Size of 2012-15 Alliances With \$50M+ in Payments (\$M)*



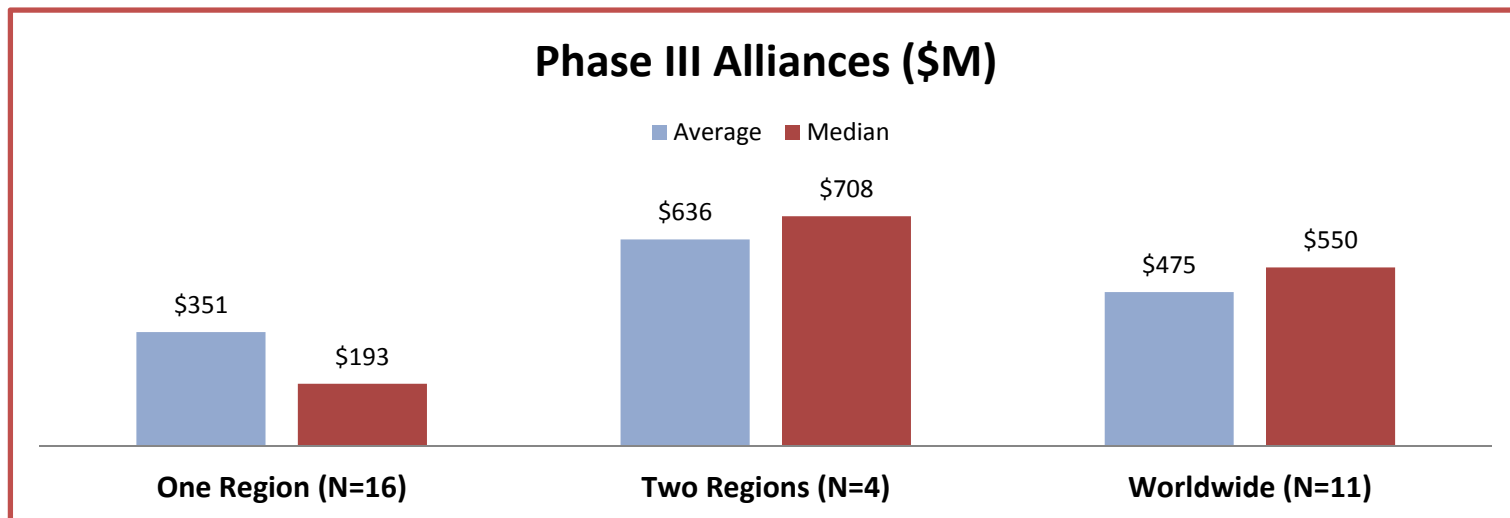
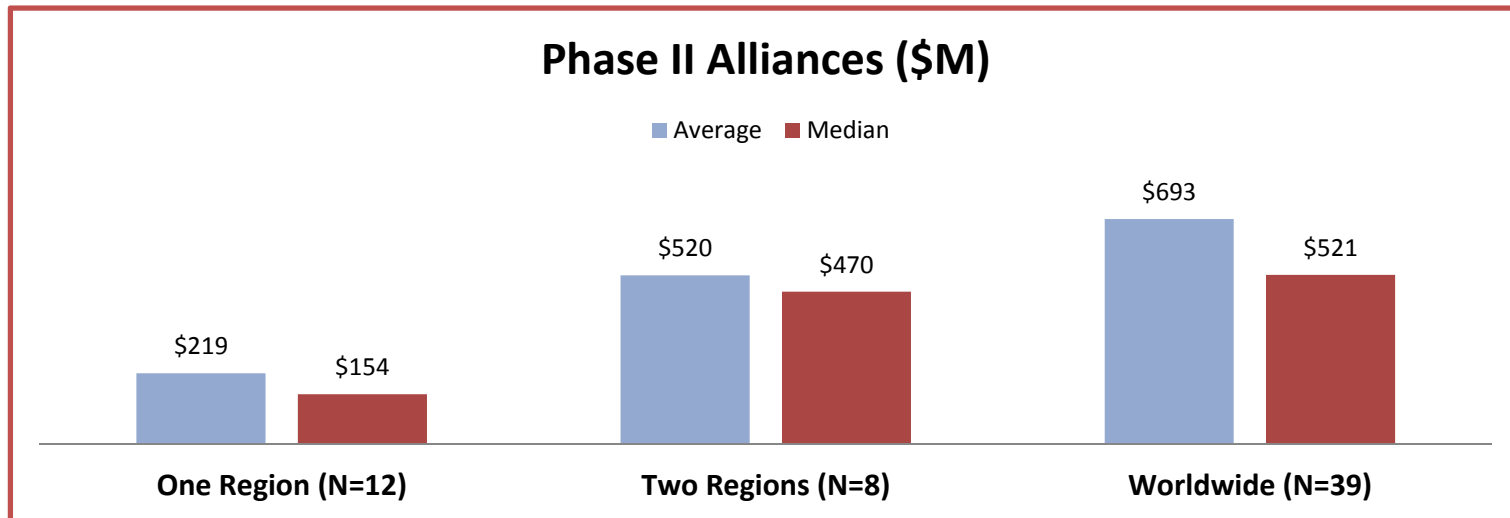
* Alliances include Research, Development, Co-Development, Joint Venture, Distribution & License Relationships; Payments include Upfront, Equity, Dev/Reg Milestones & Sales Milestones

Announced Deal Size of 2012-15 Alliances With \$50M+ in Payments (\$M)*



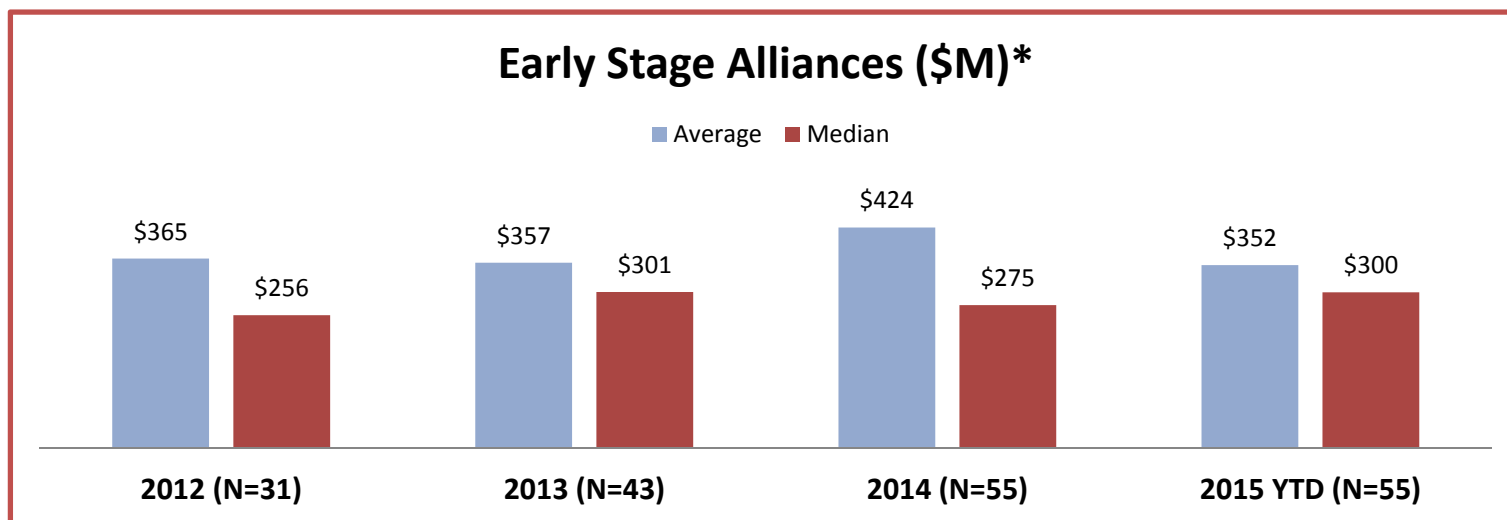
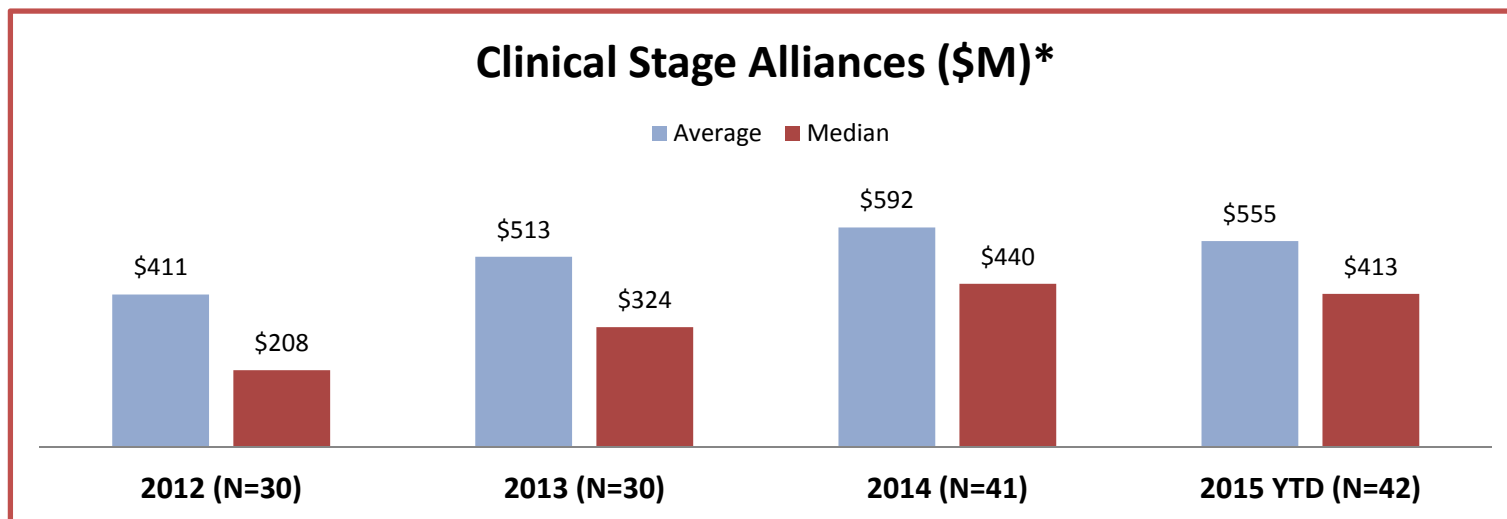
* Payments include Upfront, Equity, Dev/Reg Milestones
& Sales Milestones

Announced Deal Size of 2012-15 Alliances, By Region*



*Regions are: NAFTA (US), Europe (EU), and Asia (Japan)

Announced Deal Size of 2012-15 Alliances, By Year

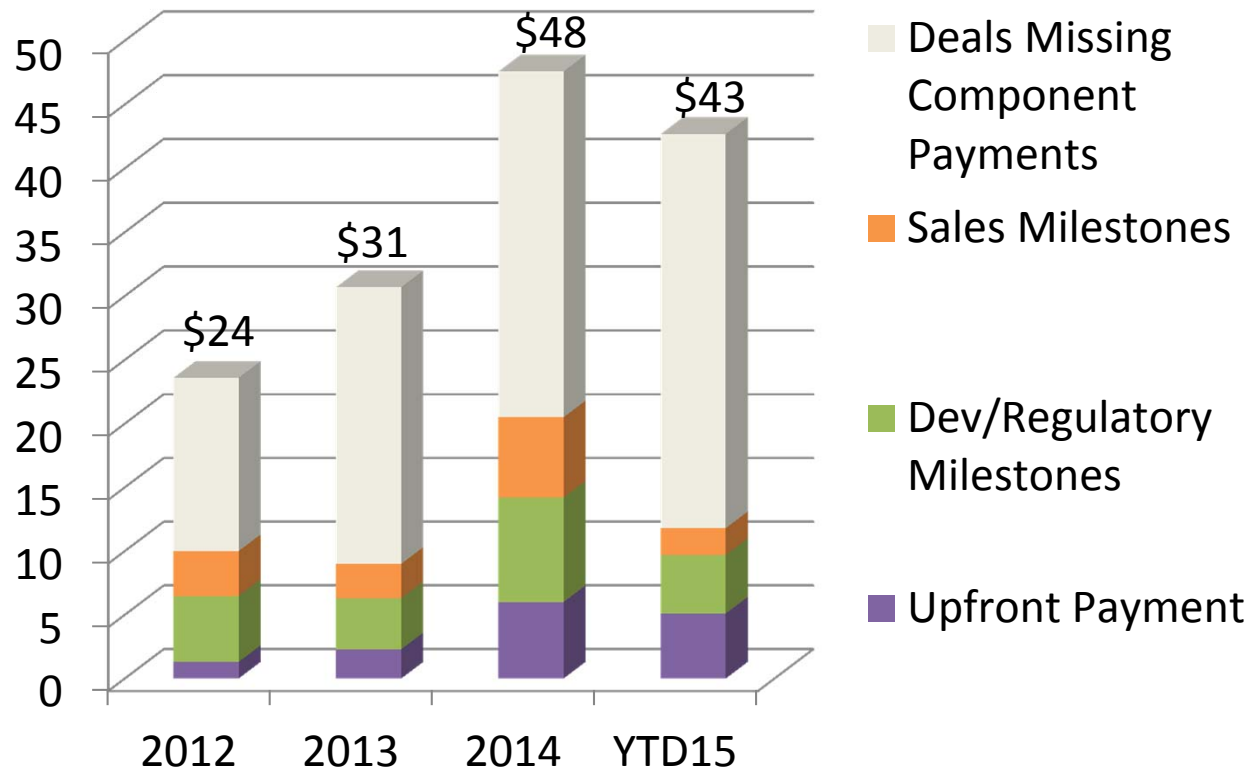


* Clinical Stage = Ph I, II & III; Early Stage = Disc, Lead, Preclin

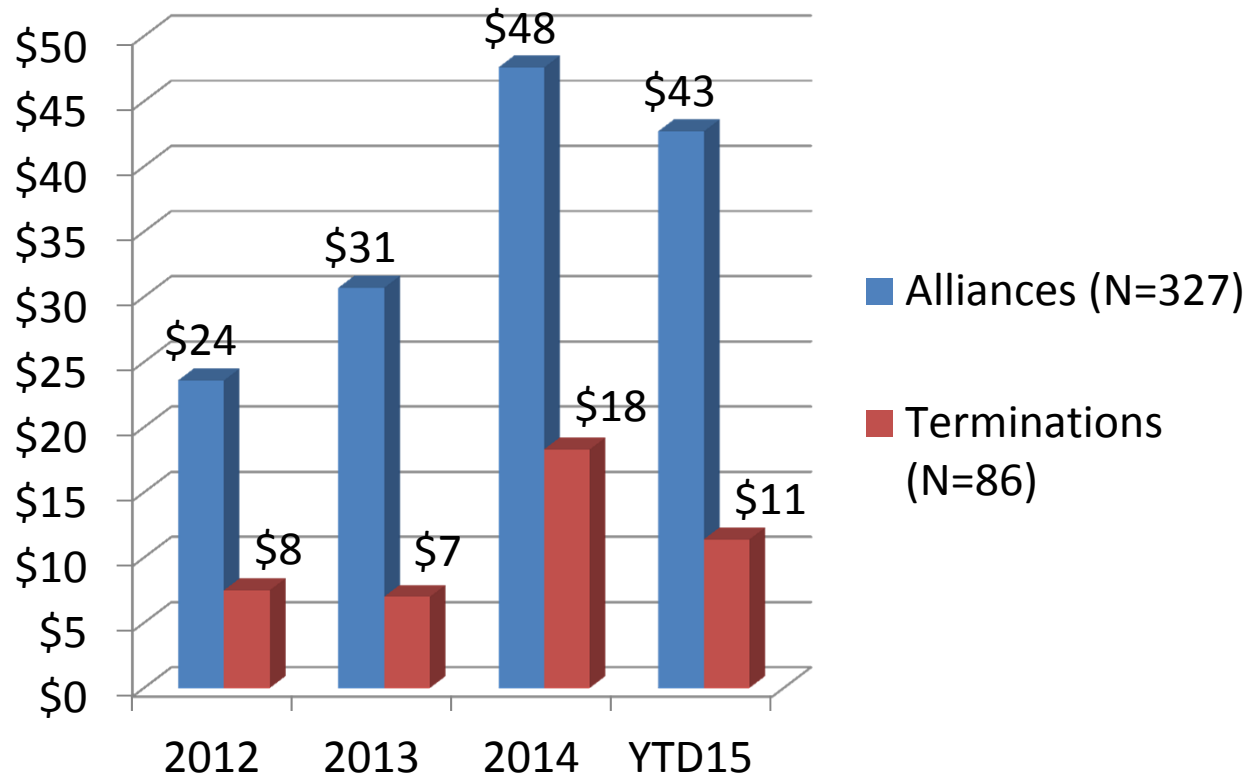
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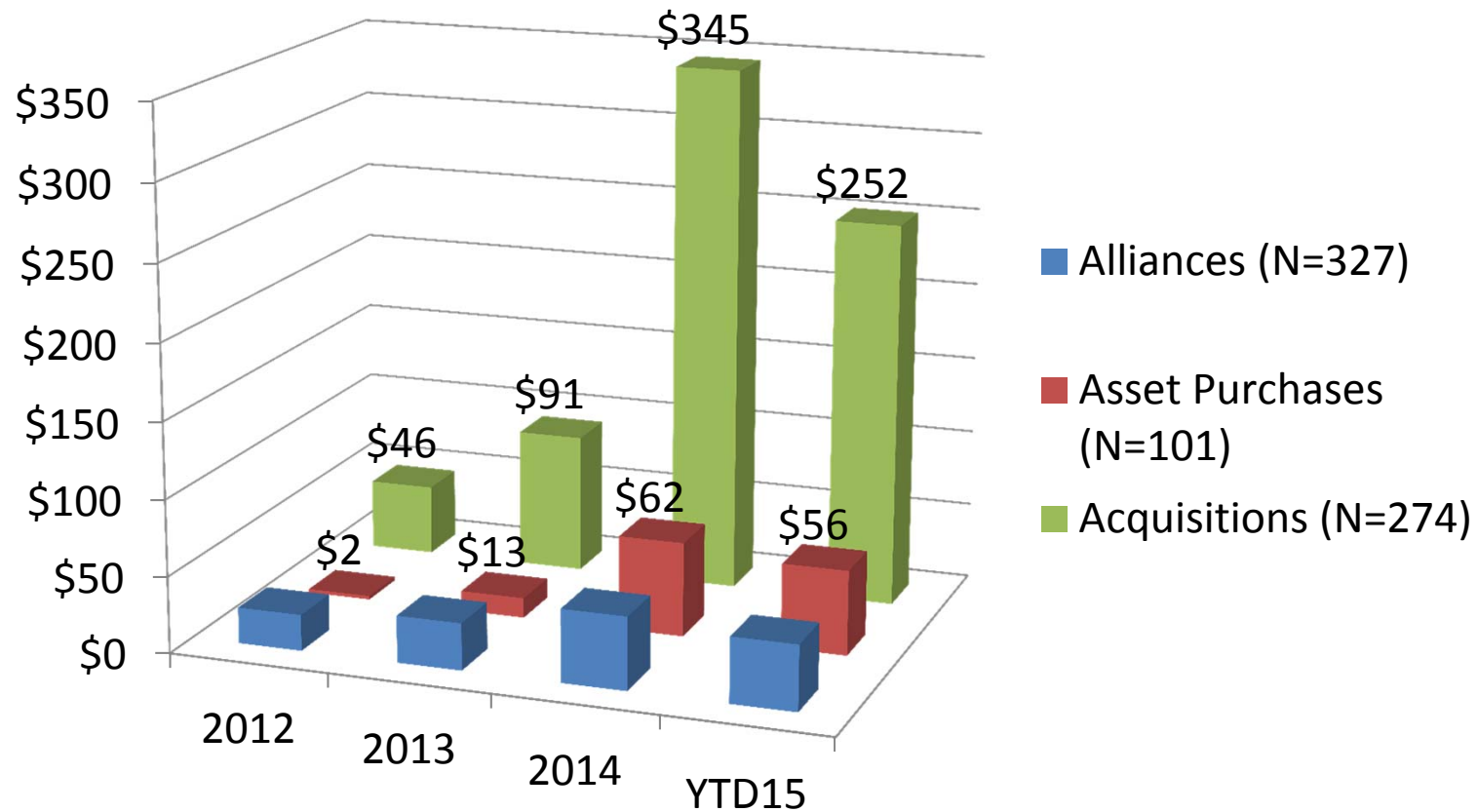
\$145 Billion in Aggregate Announced Alliance Payments for 2012-15 Alliances with \$50M+ in Payments



\$145 Billion in Announced Alliance Payments Vs. \$44 Billion in Terminated Alliances Over the Same Period



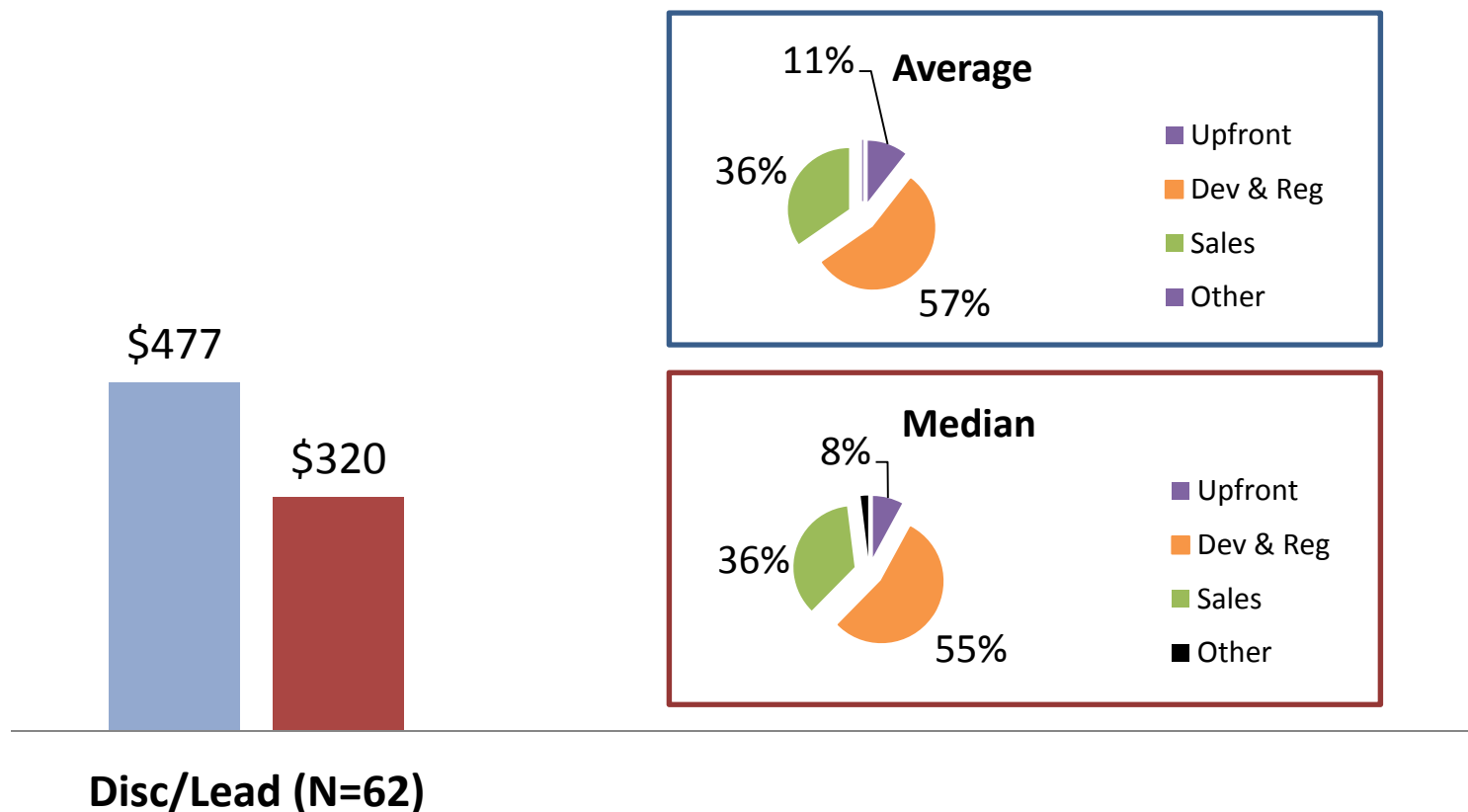
\$145 Billion in Announced Alliance Payments Vs. \$131 Billion in Asset Purchases & \$734 Billion in Acquisitions



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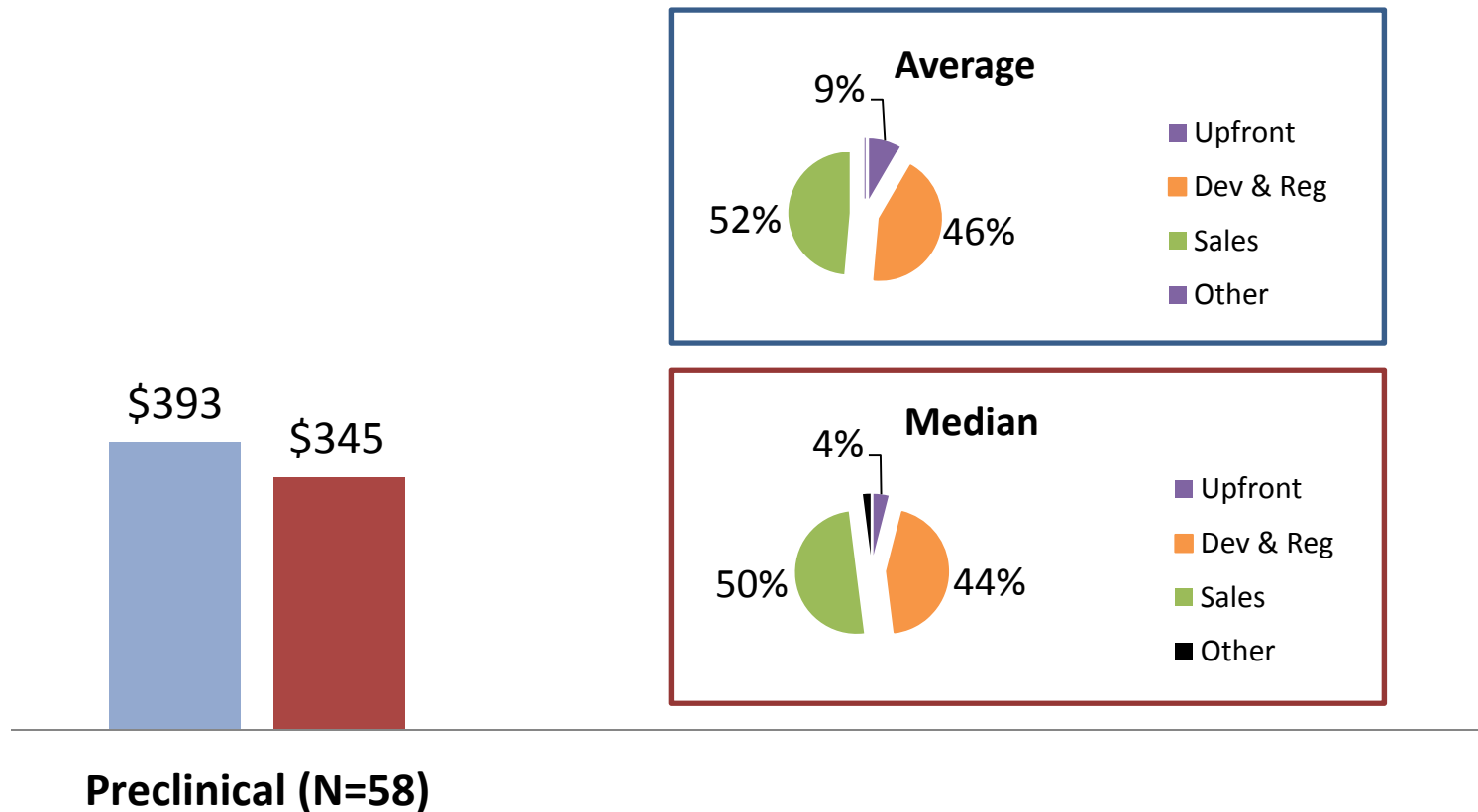
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Components of Payments for 2012-15 Alliances With \$50M+ in Payments (\$M) – Discovery/Lead Deals*



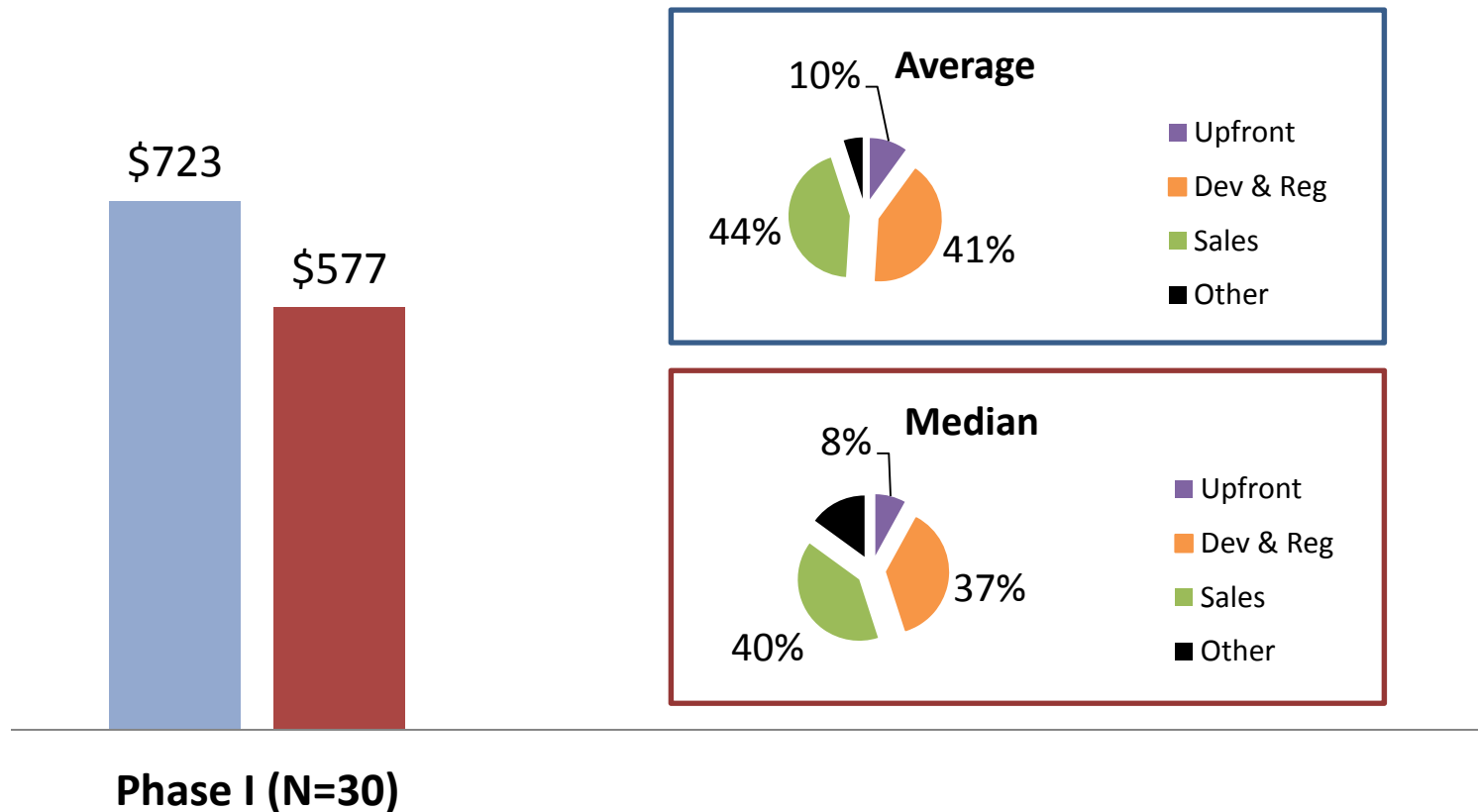
* Alliances are those for which some breakdown of payments is available (typically from 10-Ks); Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones

Components of Payments for 2012-15 Alliances With \$50M+ in Payments (\$M) – Preclinical Deals*



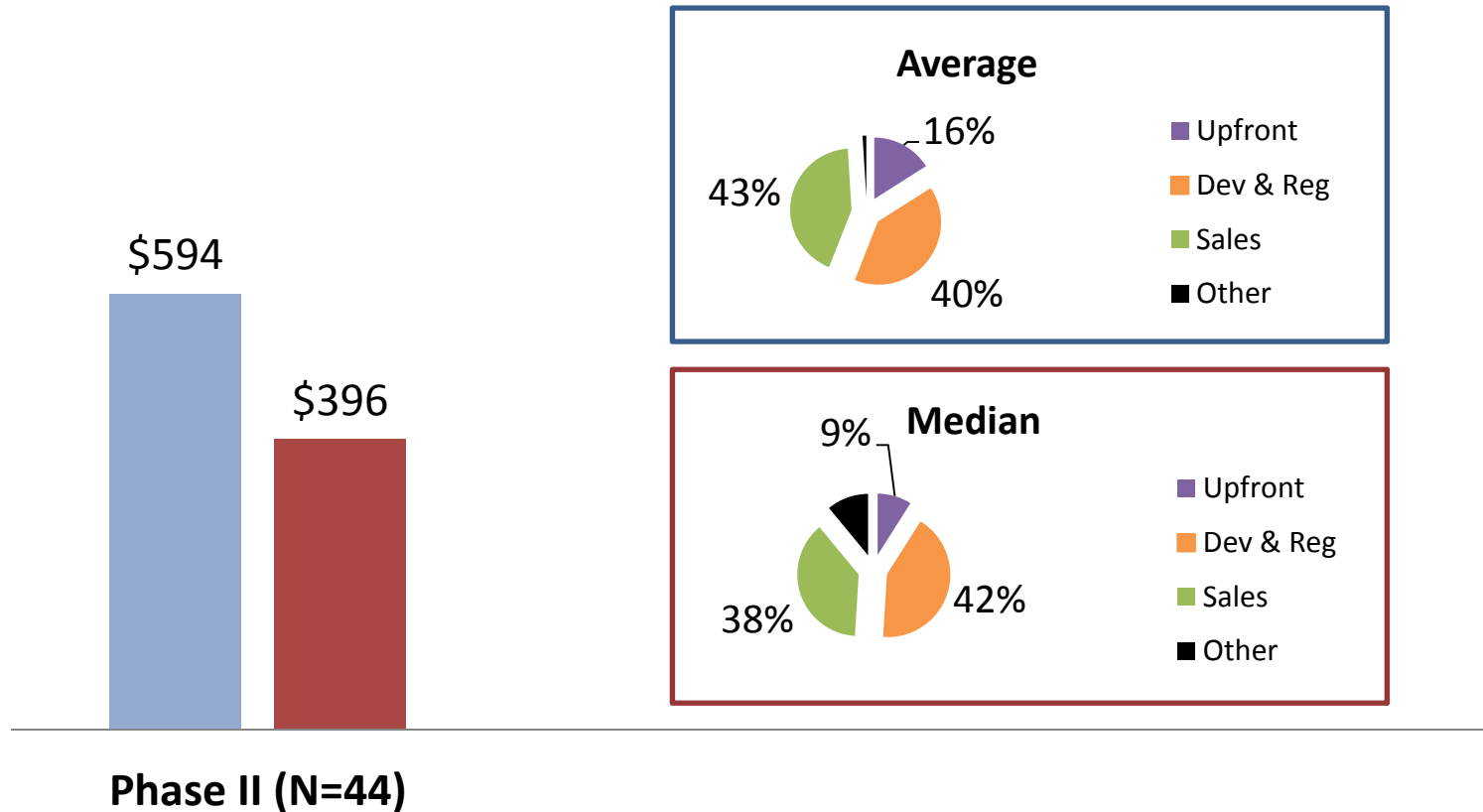
* Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones

Components of Payments for 2012-15 Alliances With \$50M+ in Payments (\$M) – Phase I Deals*



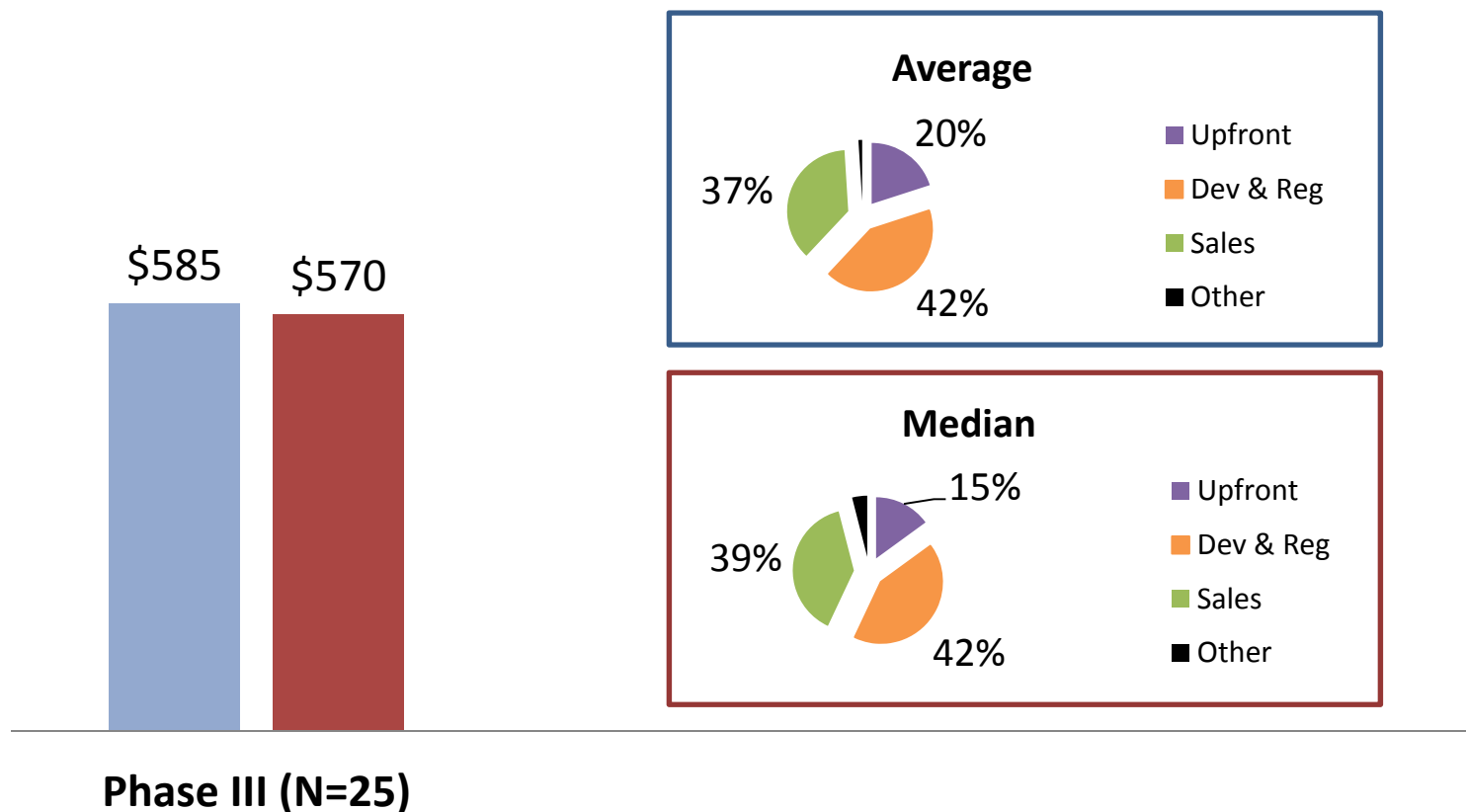
* Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones

Components of Payments for 2012-15 Alliances With \$50M+ in Payments (\$M) – Phase II Deals*



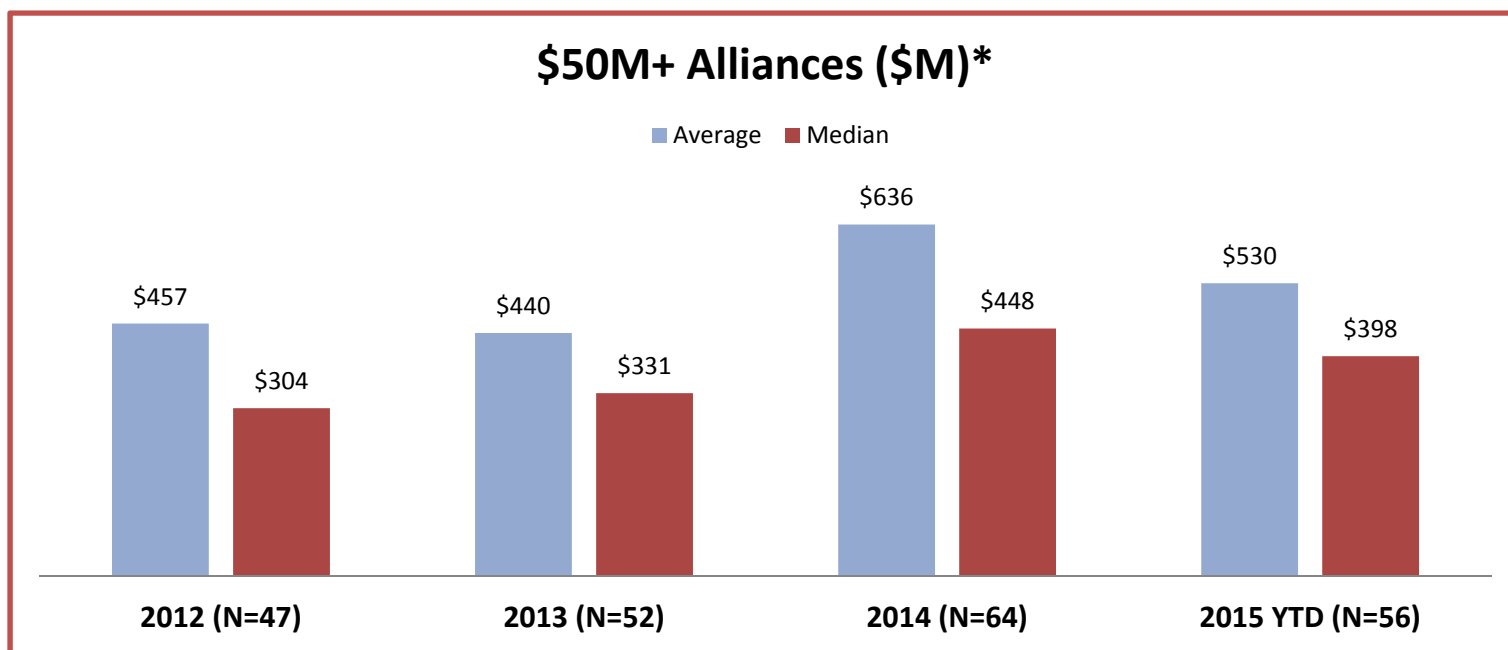
* Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones

Components of Payments for 2012-15 Alliances With \$50M+ in Payments (\$M) – Phase III Deals*



* Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones

Components of Payments for 2012-15 Alliances, By Year

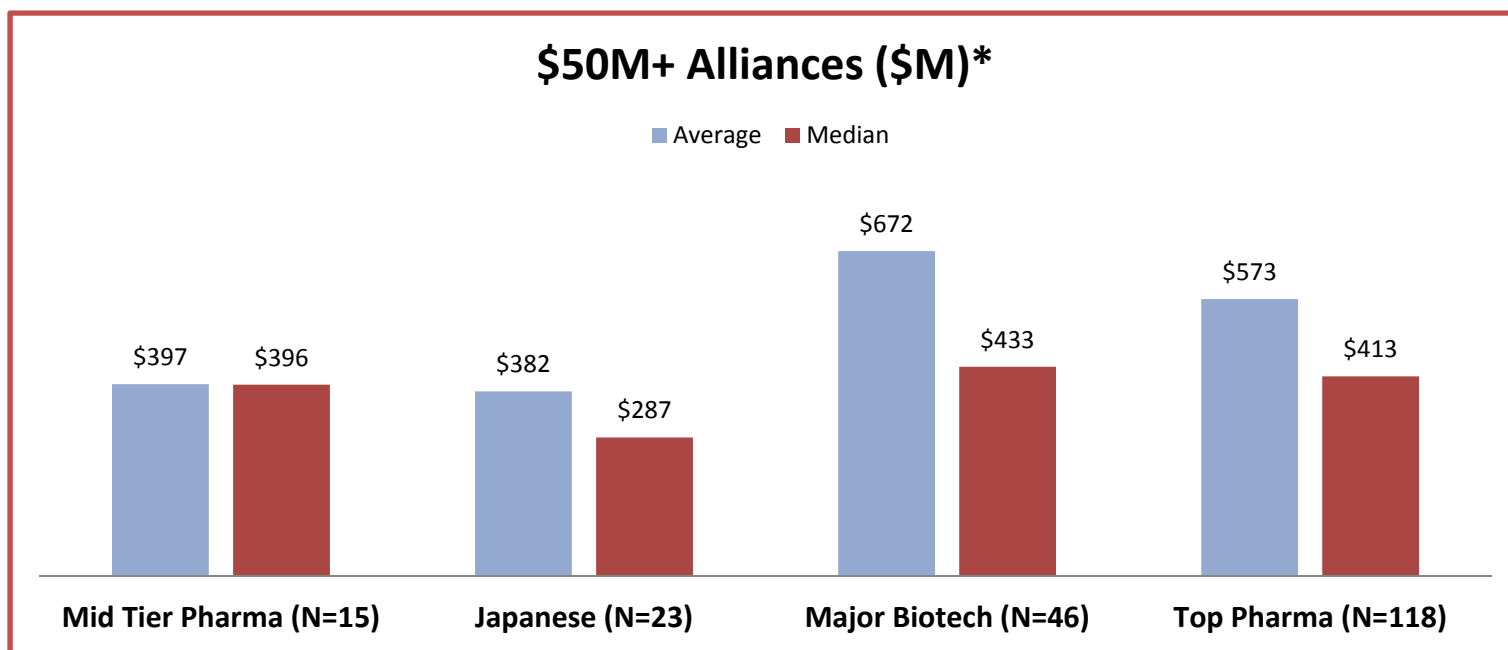


	Average	Median		Average	Median		Average	Median		Average	Median
Upfront	6.7%	4.8%		12.1%	6.2%		13.3%	8.2%		16.3%	10.9%
Dev/Reg	45.4%	45.5%		46.9%	44.4%		44.0%	44.6%		50.6%	45.1%
Sales	45.2%	48.3%		43.4%	40.1%		40.1%	38.9%		39.2%	31.6%

* Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones



Components of Payments for 2012-15 Alliances, By Partner



	Average	Median		Average	Median		Average	Median		Average	Median
Upfront	21.1%	10.4%		14.1%	8.9%		20.3%	10.3%		12.1%	7.0%
Dev/Reg	40.5%	28.6%		37.9%	36.4%		48.8%	50.3%		49.5%	49.1%
Sales	40.1%	44.9%		49.1%	49.4%		34.7%	30.8%		39.1%	38.1%

* Payment Component Categories are: Upfront & Equity, Dev/Reg Milestones, Sales Milestones

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Applying Effective Royalty Rate (EFR) Analysis

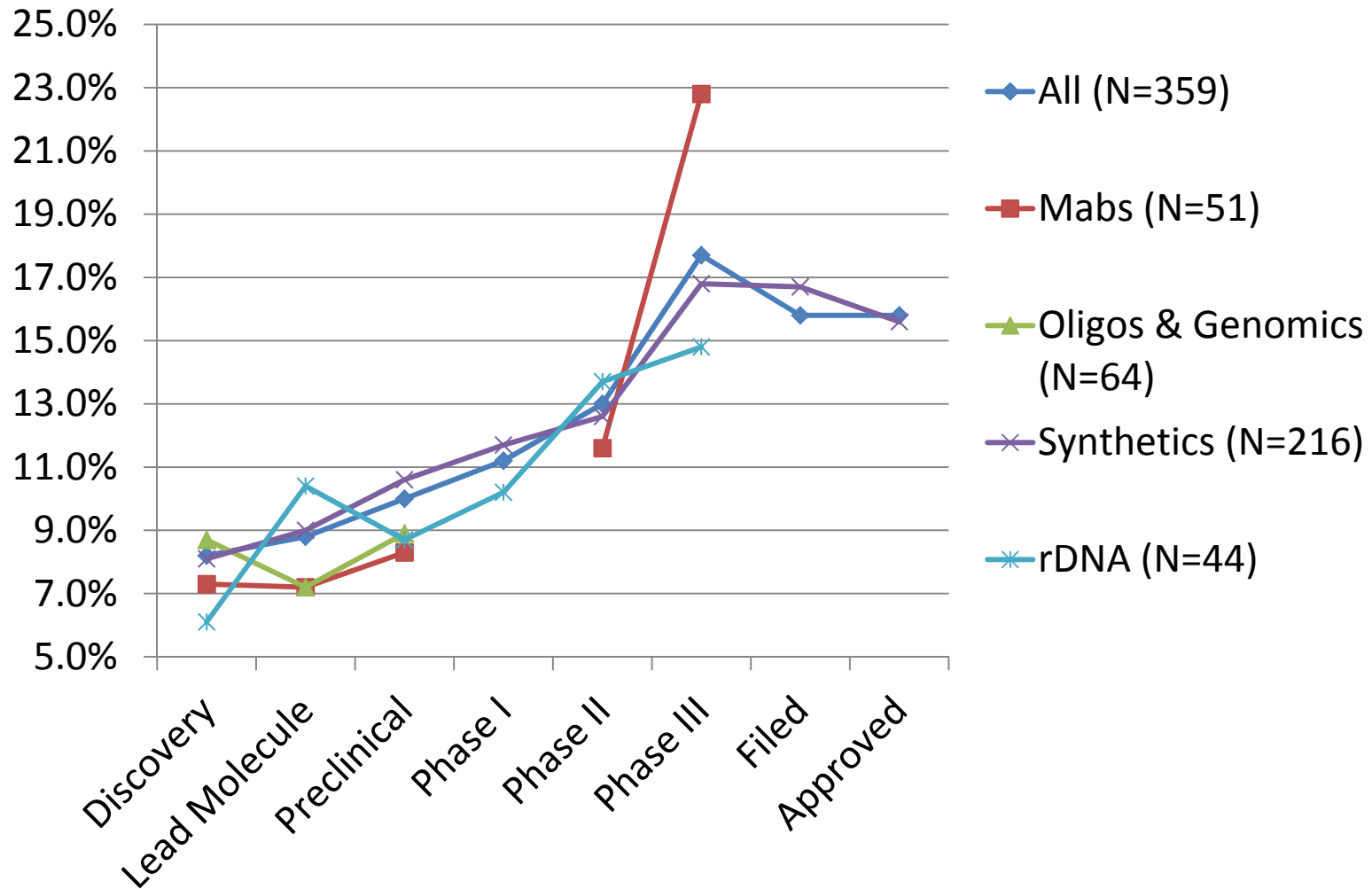
- If a license calls for 8% royalty on the first \$100M in annual sales, then 10% to \$500M, then 15% on sales above \$500M/yr, the EFR would be 9.6% on \$500M in Assumed Sales:

\$ 8M on \$100M

\$40M on \$400M

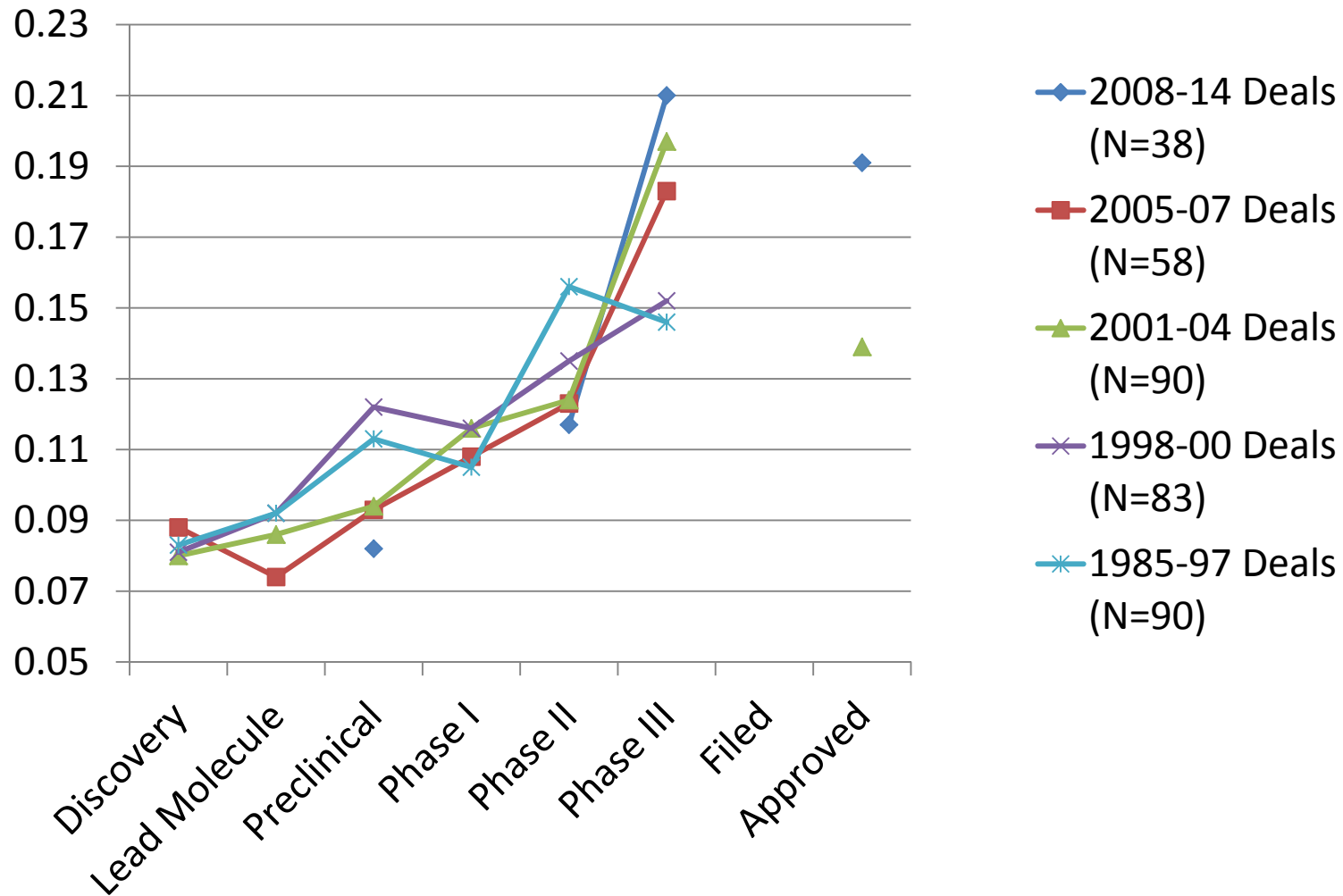
\$48M on \$500M = 9.6% EFR

Effective Royalty Rate of Alliances by Technology*



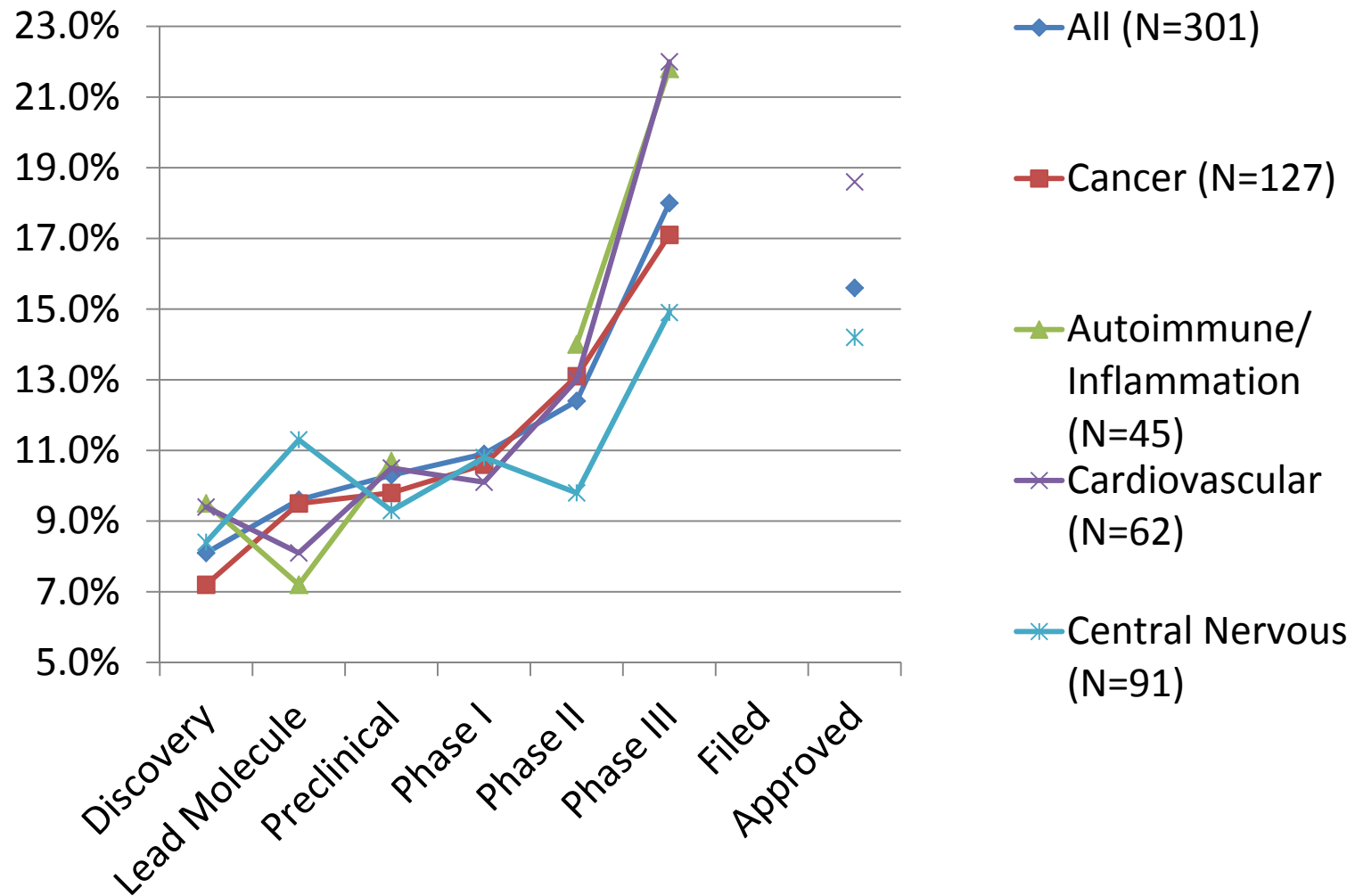
* Effective Royalty Rate (EFR) calculated for assumed annual sales of \$500M/yr, based on Biopharma deals obtained via FOIA

Effective Royalty Rate of Technology Alliances by Year*



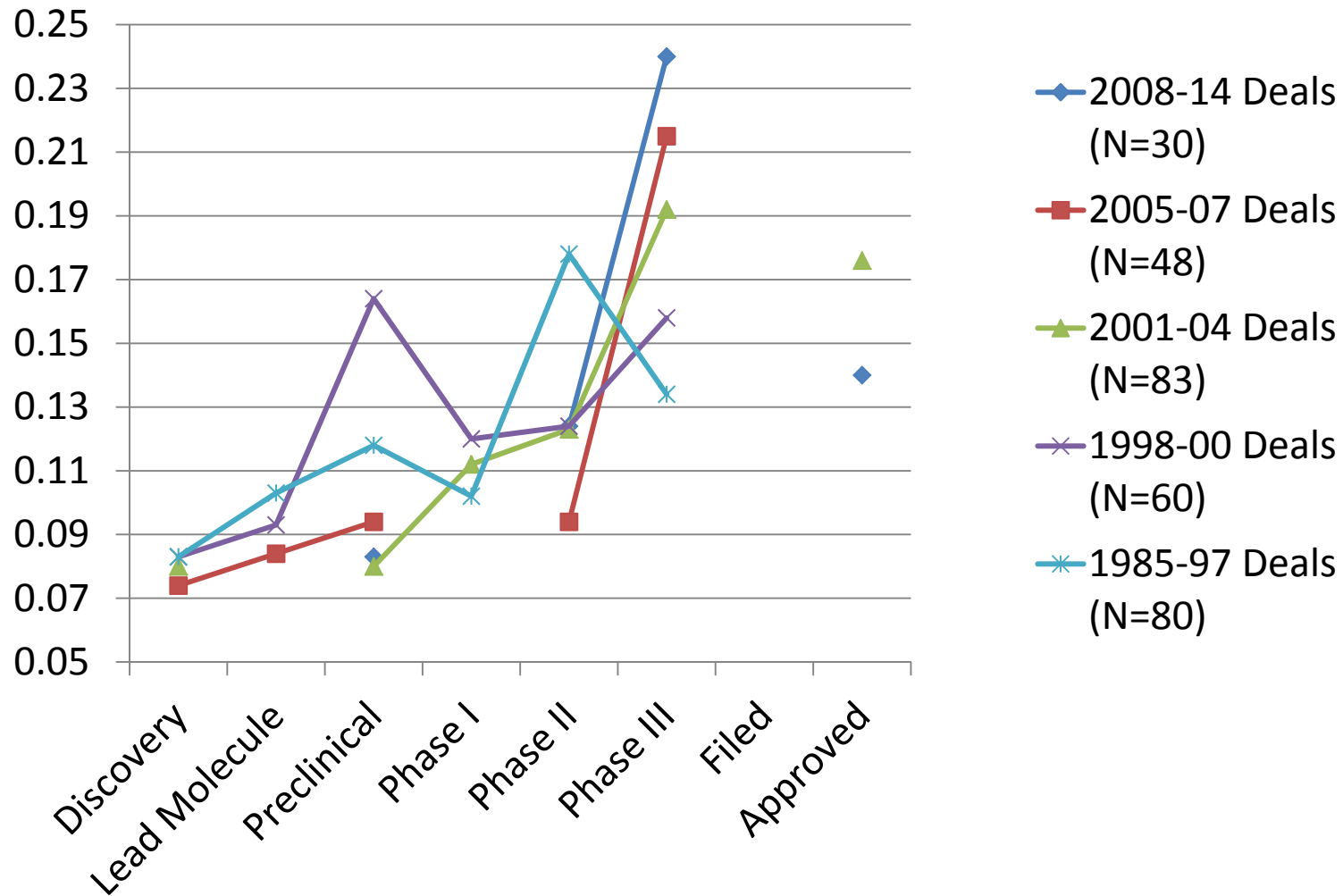
* Effective Royalty Rate (EFR) calculated for assumed annual sales of \$500M/yr, based on Biopharma deals obtained via FOIA

Effective Royalty Rate of Alliances by Therapeutic Area*



* Effective Royalty Rate (EFR) calculated for assumed annual sales of \$500M/yr, based on Biopharma deals obtained via FOIA

Effective Royalty Rate of Therapeutic Area Alliances by Year*



* Effective Royalty Rate (EFR) calculated for assumed annual sales of \$500M/yr, based on Biopharma deals obtained via FOIA

BioSciBD.com has an Analysis of 1,100+ Royalty Term Provisions

Duration of Royalty Obligations: 'Til Death Do Us Part?

MARK EDWARDS

OCTOBER 23, 2015

BioSci has undertaken an analysis of royalty term provisions in hopes that future biopharma alliances might add clarity to this crucial aspect of the deal negotiation.

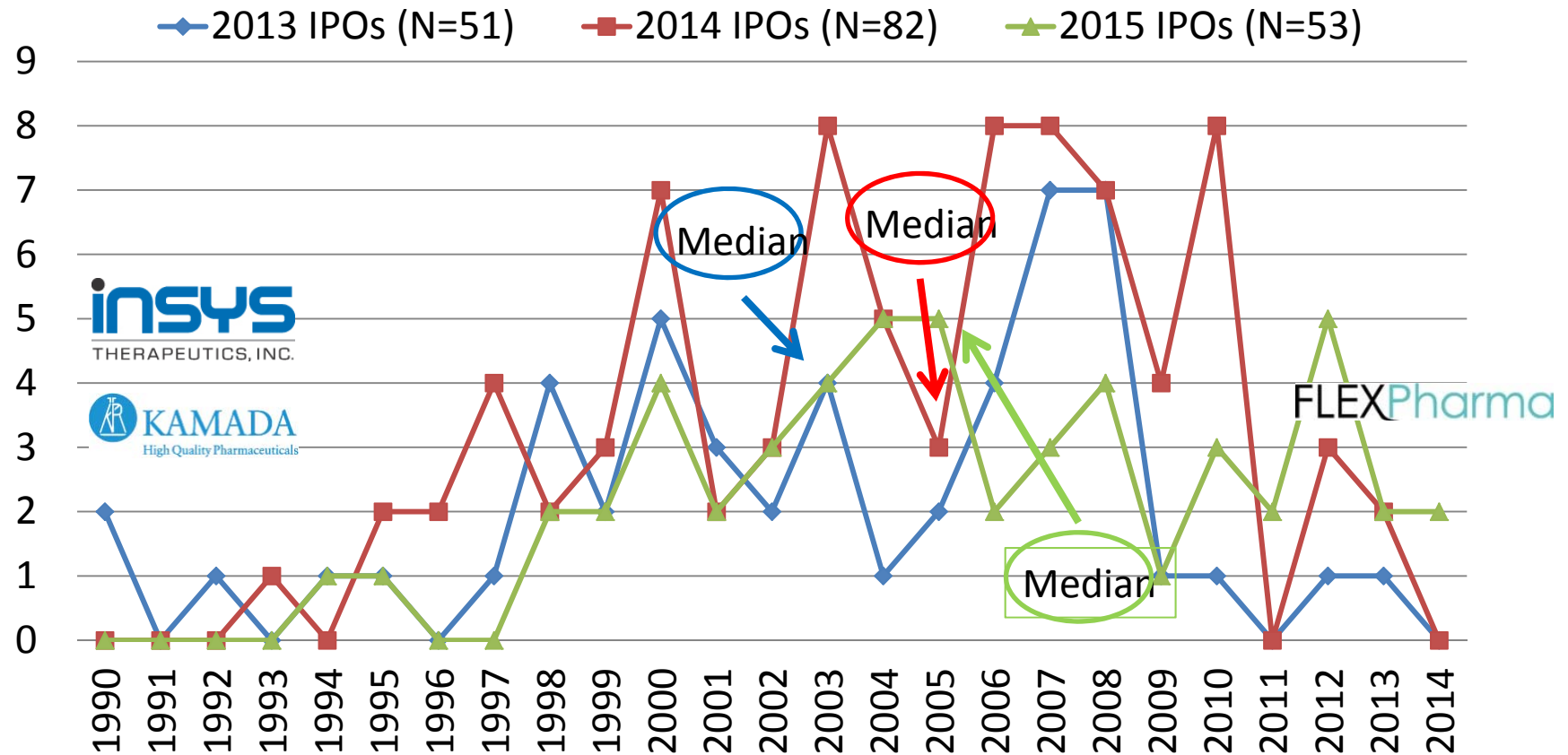
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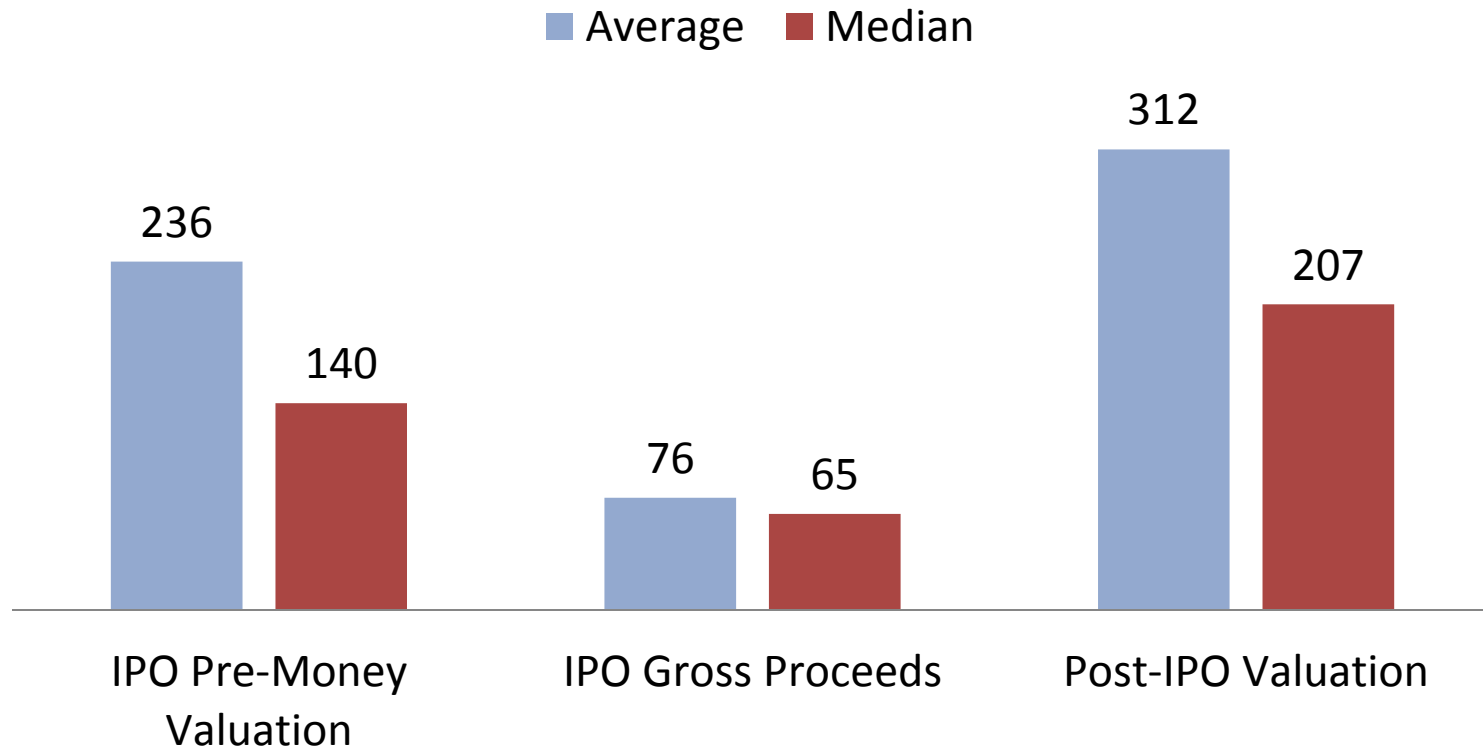
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186 Biotechs Went Public in US

From Jan 2013 Thru Mid-October 2015, by Founding Year

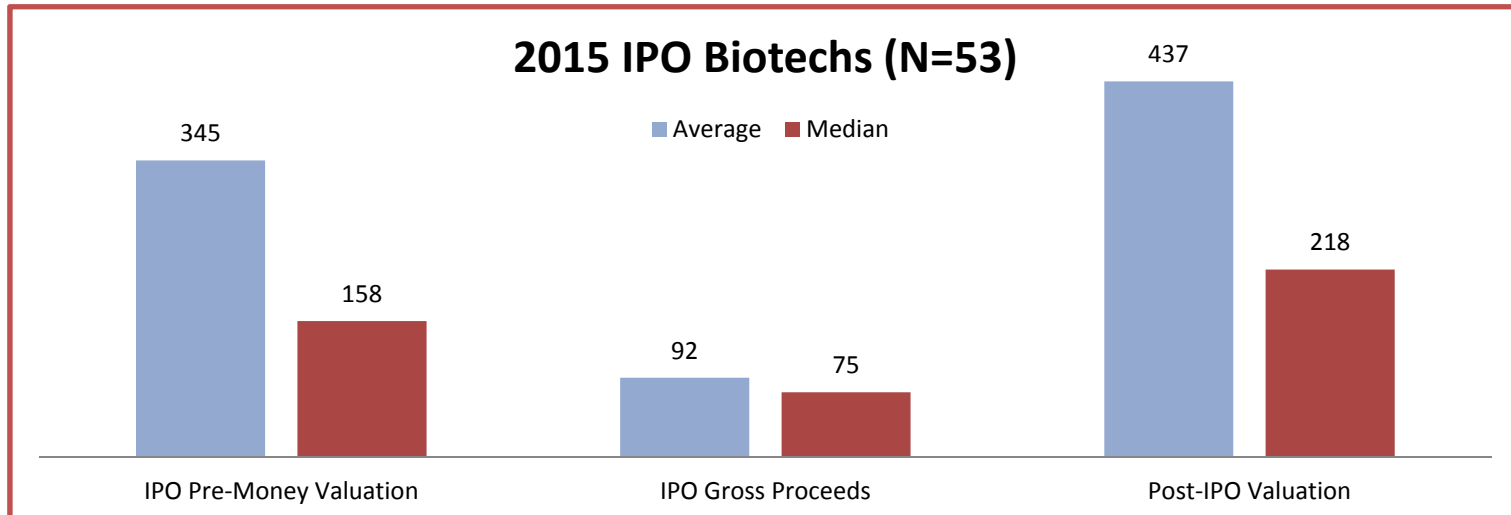
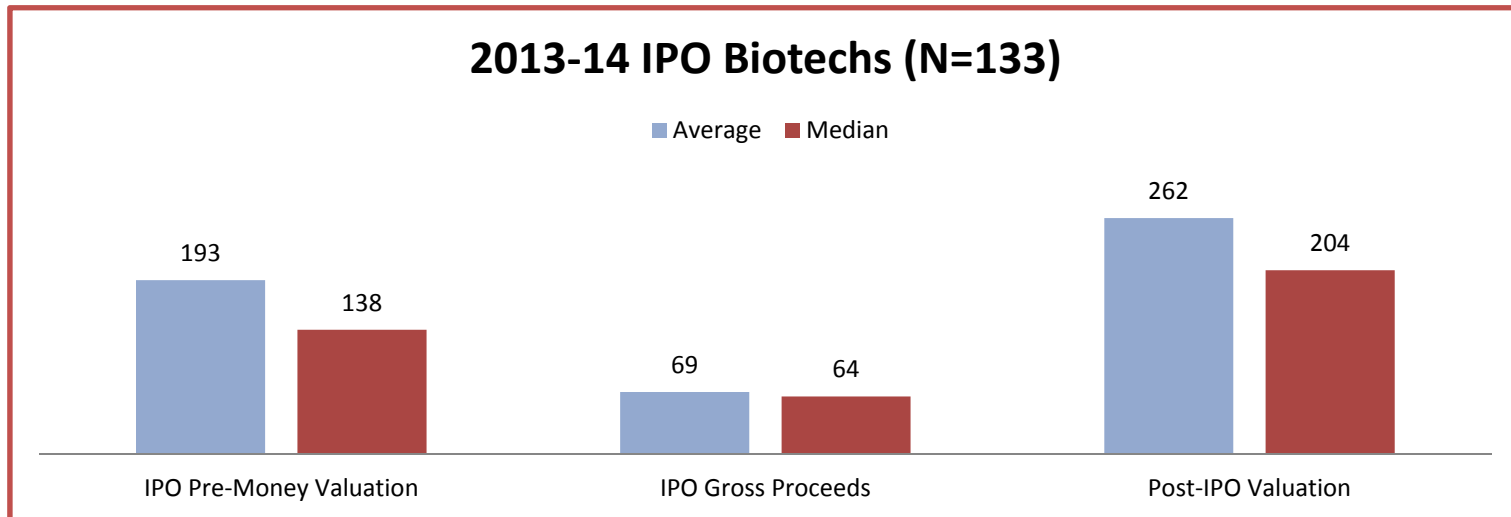


2013-2015 Biotech IPO Class: Valuation at IPO (\$M)*



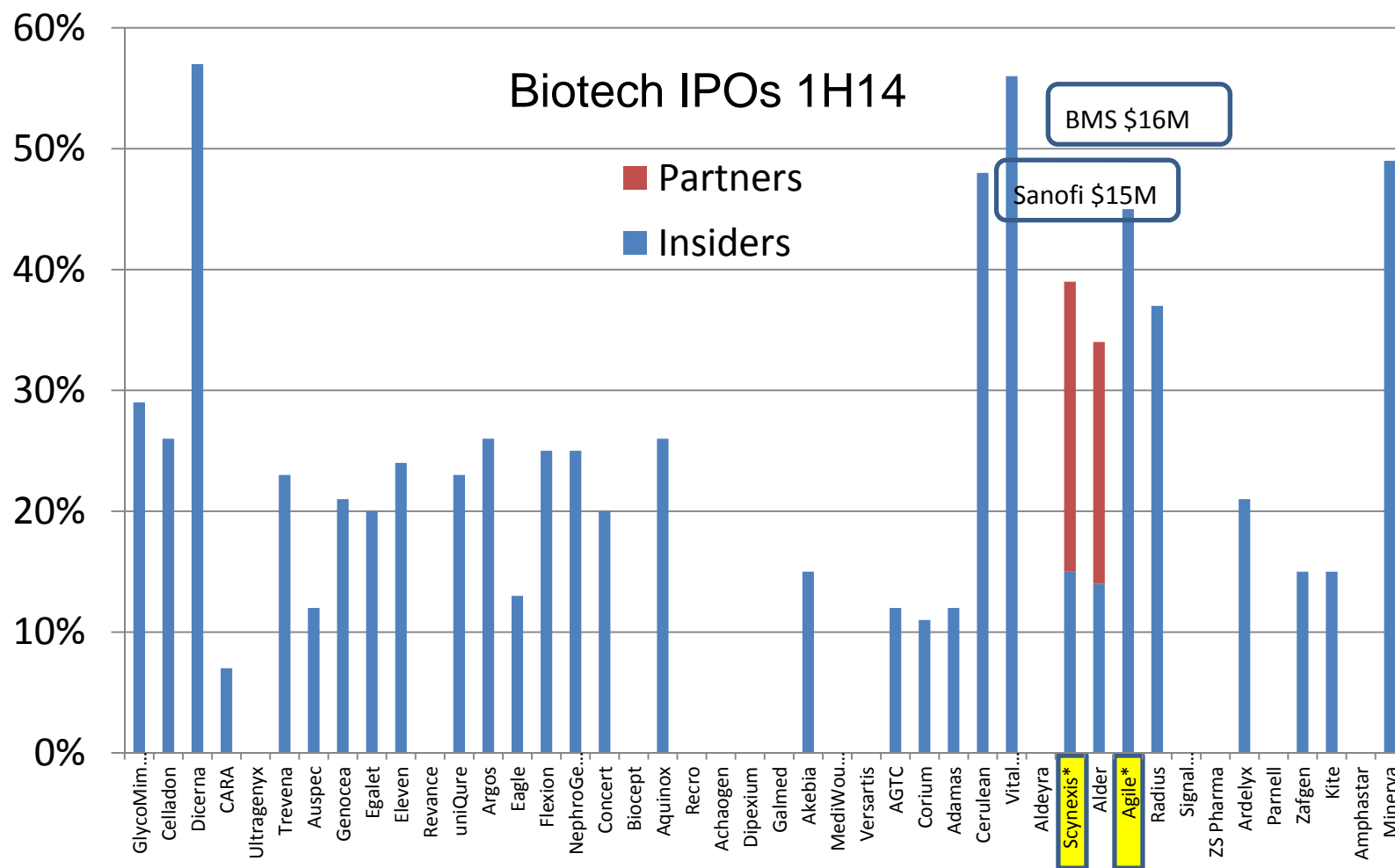
* 186 US Biotech IPOs, \$14.1B in Aggregate IPO Gross Proceeds

2013-14 IPO Biotechs Vs. 2015 IPO Biotechs*



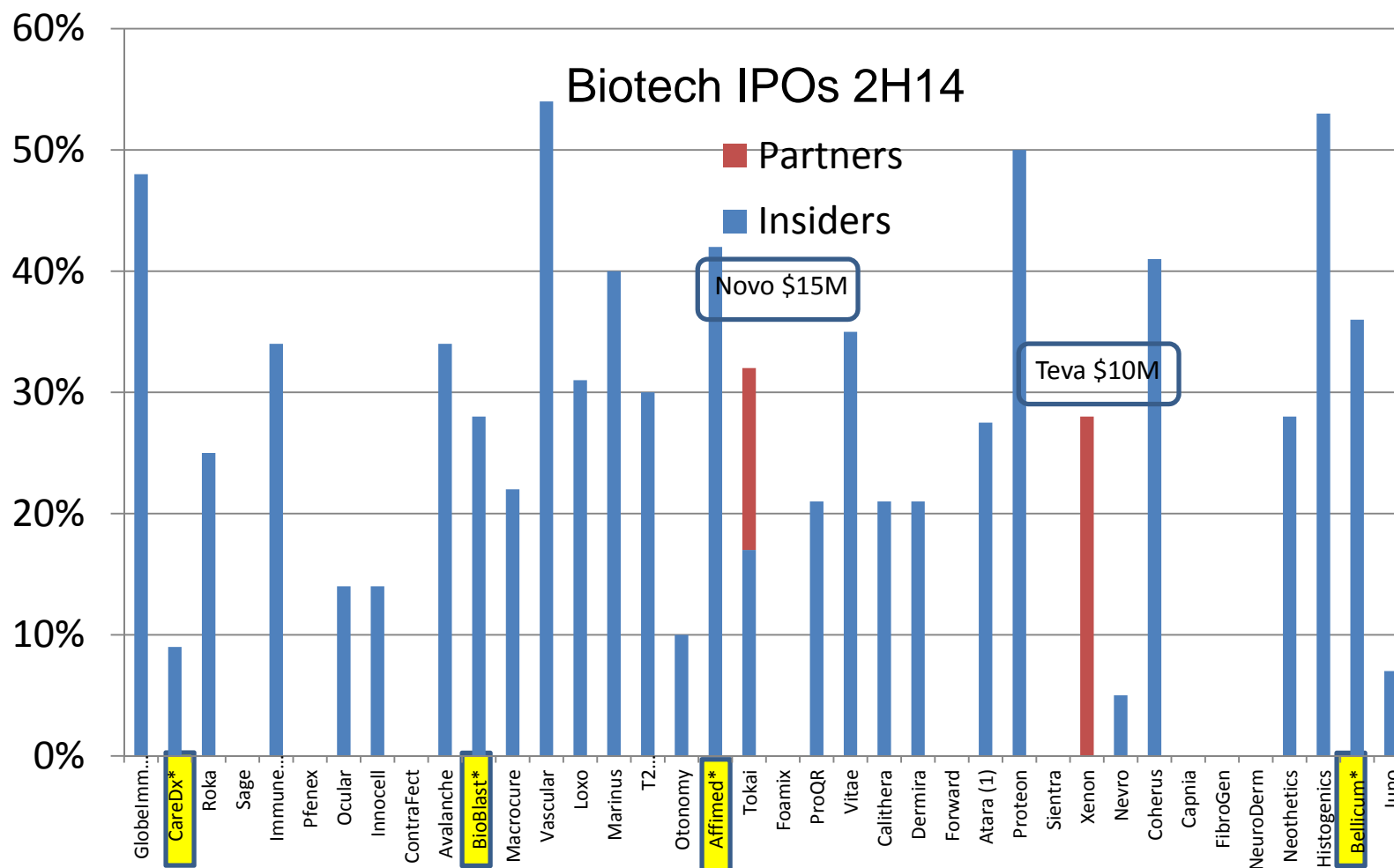
* 133 US Biotech IPOs in 2013-14, \$9.2B in Aggregate IPO Gross Proceeds; 53 US Biotech IPOs to 10/15/15, \$4.9B in Aggregate IPO Gross Proceeds

PreSelling the IPO & Increasing the Bankers' Fee – 1 of 4



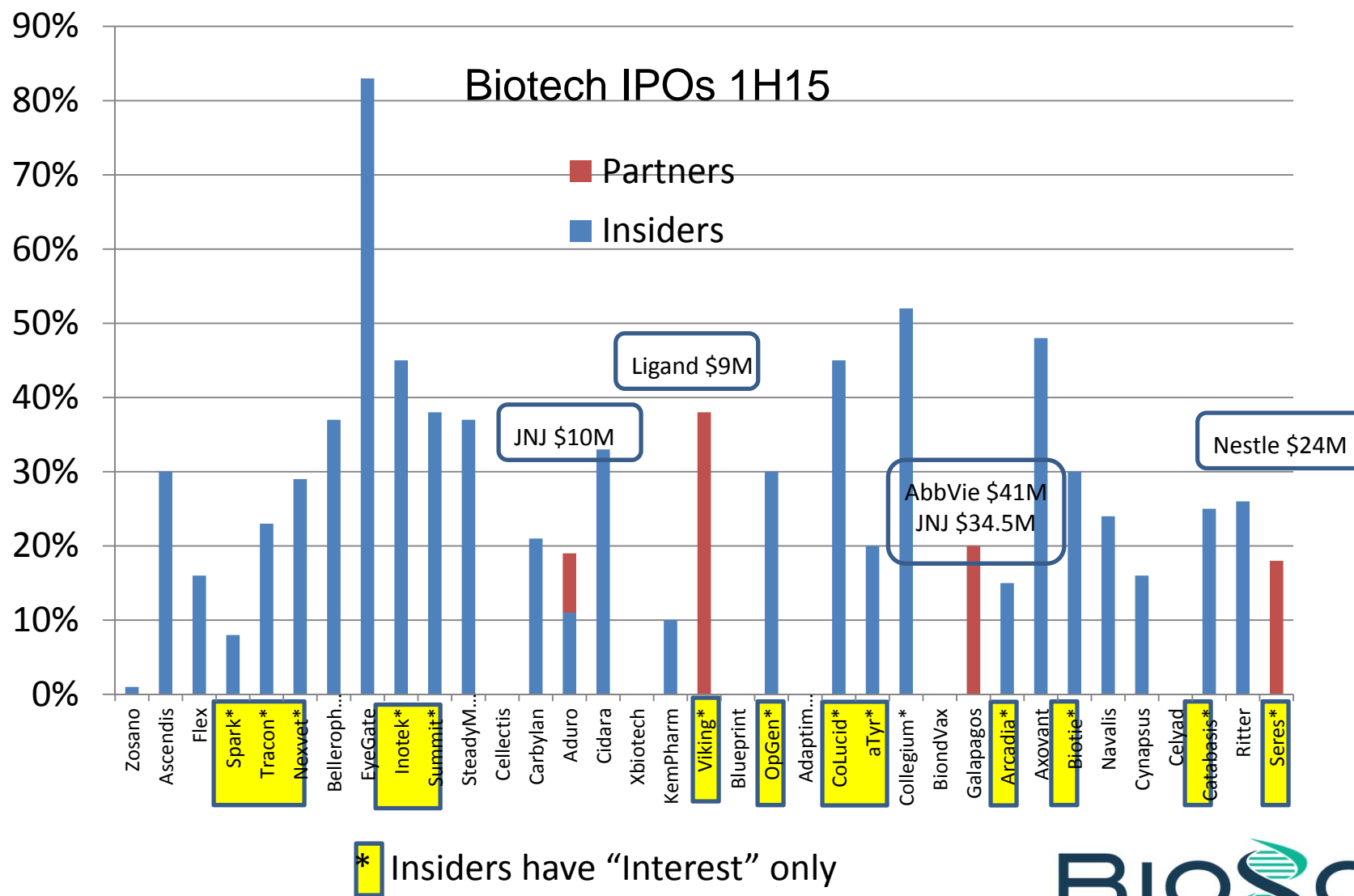
* Insiders have "Interest" only

PreSelling the IPO & Increasing the Bankers' Fee – 2 of 4

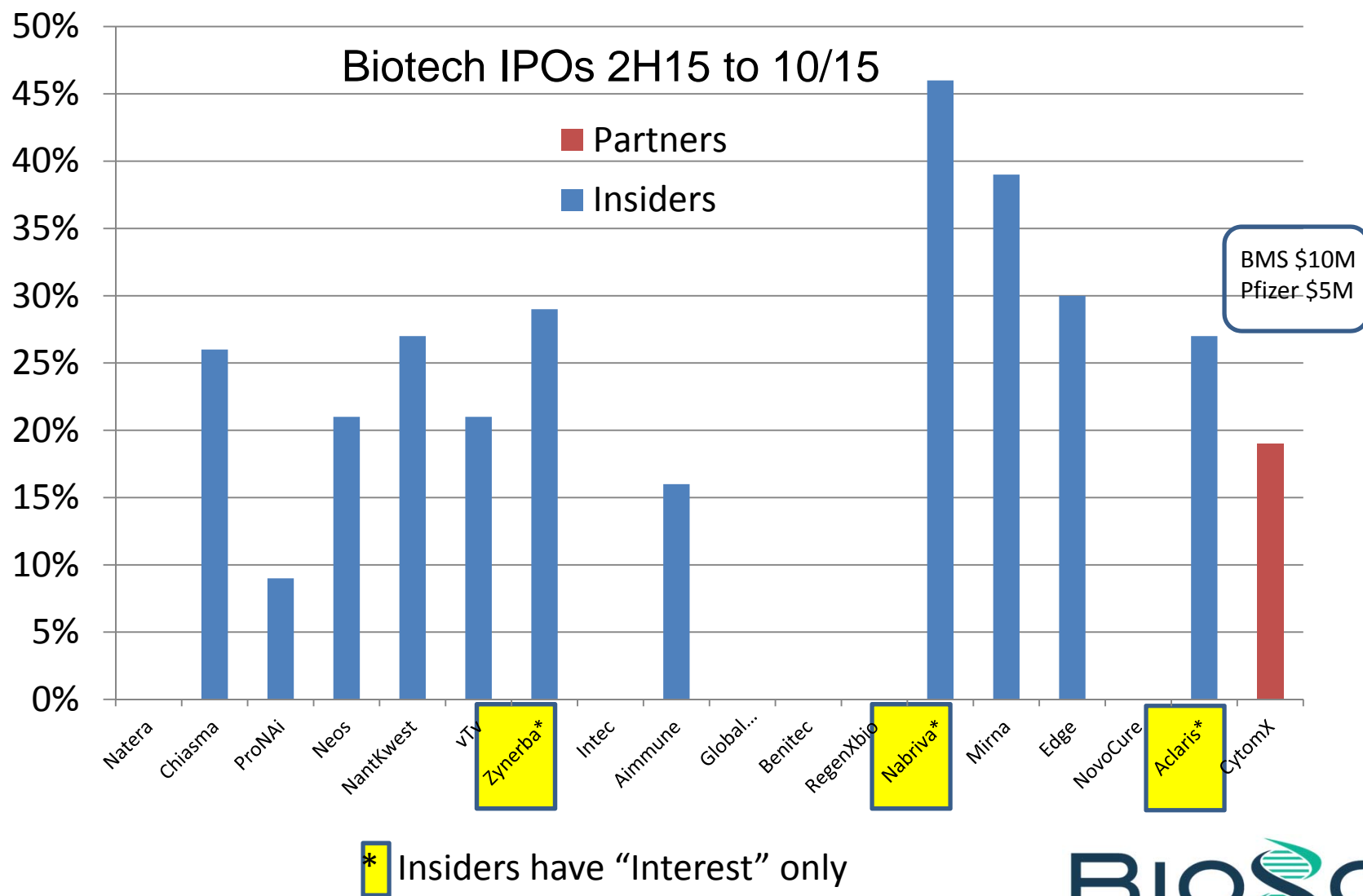


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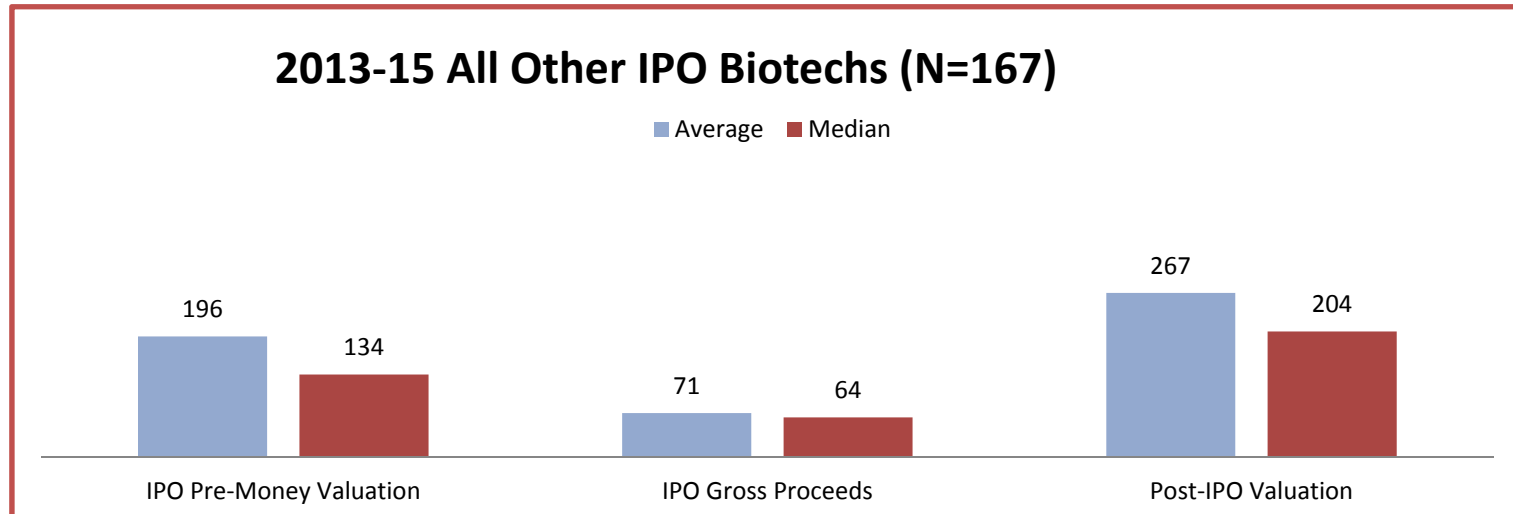
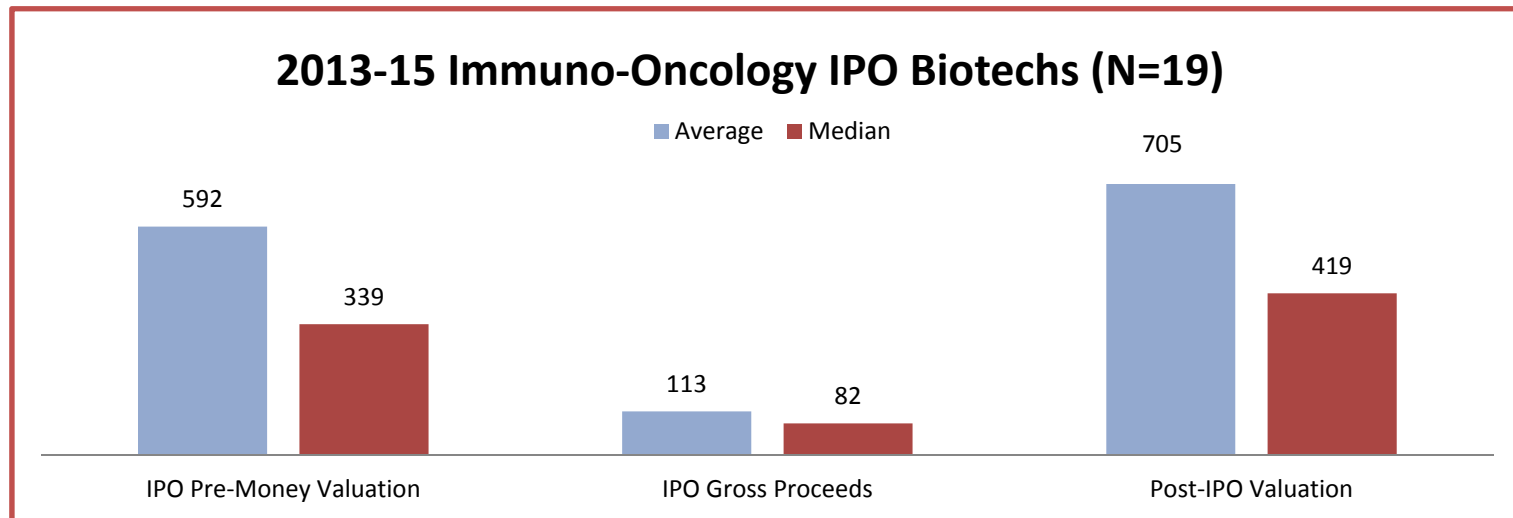
PreSelling the IPO & Increasing the Bankers' Fee – 3 of 4



PreSelling the IPO & Increasing the Bankers' Fee – 4 of 4



Immuno-Oncology IPO Biotechs Vs. All Other IPO Biotechs*



* 19 US Immuno-Oncology Biotech IPOs in 2013-15, \$2.1B in Aggregate IPO Gross Proceeds; 167 Other US Biotech IPOs in 2013-15, \$11.9B in Aggregate IPO Gross Proceeds

Immuno-Oncology IPO Biotech Mkt Caps are Up by 57%

Biotech	IPO Date	Ticker	Date Founded	Most Advanced	IPO Proceeds	IPO Pre-Money	Post IPO Mkt Cap	10/23/15 Mkt Cap	Percent Change
Bluebird	18-Jun-13	BLUE	1992	Preclinical	\$101	\$287	\$388	\$3,010	677%
OncoMed	17-Jul-13	OMED	2004	Phase I	\$82	\$379	\$461	\$566	23%
Five Prime	18-Sep-13	FPRX	2001	Phase I	\$62	\$146	\$208	\$770	270%
MacroGenics	09-Oct-13	MGNX	2000	Phase II	\$80	\$304	\$384	\$1,010	163%
Xencor	02-Dec-13	XNCR	1997	Phase I	\$70	\$92	\$162	\$485	200%
TetraLogic	11-Dec-13	TLOG	2001	Phase I	\$50	\$98	\$148	\$41	-72%
Kite	19-Jun-14	KITE	2009	Phase I/II	\$128	\$500	\$627	\$3,090	393%
Immune Design	23-Jul-14	IMDZ	2008	Phase I	\$60	\$130	\$190	\$264	39%
Affimed	12-Sep-14	AFMD	2000	Phase I	\$56	\$112	\$168	\$205	22%
Vitae	24-Sep-14	VTAE	2001	Phase II	\$55	\$84	\$139	\$254	83%
Juno	18-Dec-14	JUNO	2013	Phase II	\$265	\$1,606	\$1,870	\$4,950	165%
Cellectis	24-Mar-15	CLLS	2000	Preclinical	\$228	\$1,220	\$1,448	\$912	-37%
Aduro	14-Apr-15	ADRO	2000	Phase IIb	\$119	\$884	\$1,003	\$1,500	50%
Adaptimmune	05-May-15	ADAP	2008	Phase I/II	\$191	\$1,012	\$1,204	\$687	-43%
Celyad	18-Jun-15	CYAD	2007	Phase III	\$100	\$538	\$638	\$371	-42%
NantKwest	27-Jul-15	NK	2002	Phase I	\$208	\$1,765	\$1,973	\$865	-56%
Mirna	30-Sep-15	MIRN	2007	Phase I	\$44	\$97	\$141	\$141	0%
NovoCure	01-Oct-15	NVCR	2000	Mkt	\$165	\$1,654	\$1,819	\$1,610	-12%
CytomX	07-Oct-15	CTMX	2010	Preclinical	\$80	\$339	\$419	\$339	-19%
					\$2,143		\$13,388	\$21,070	57%

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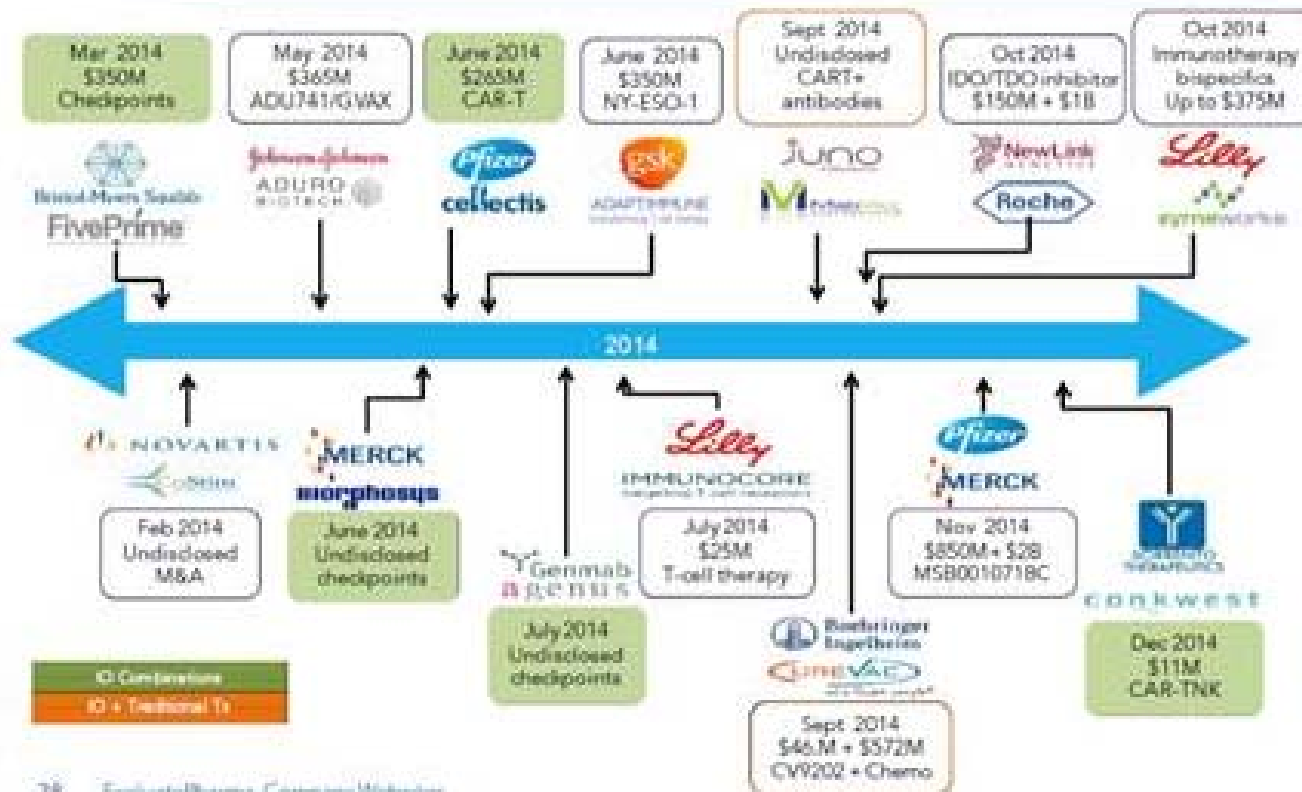
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Immuno-Oncology Has Been the Hottest Deal Ticket

- 36 Immuno-Oncology Deals Were Announced Over the Past Three Years with Upfront Payments of \$30M or More
 - \$5.8B in Aggregate Upfront Payments
 - \$32.4B in Aggregate Deal Payments
- 19 I-O Alliances Were Discovery or Preclinical Stage; 11 Were Phase I Stage; 6 Were Phase II or Phase III at Time of Signing

So Much Deal Activity, Graphics Depts Are Working Overtime

Immuno-Oncology Deal Timeline 2014



28 EvaluatePharma, Company Websites

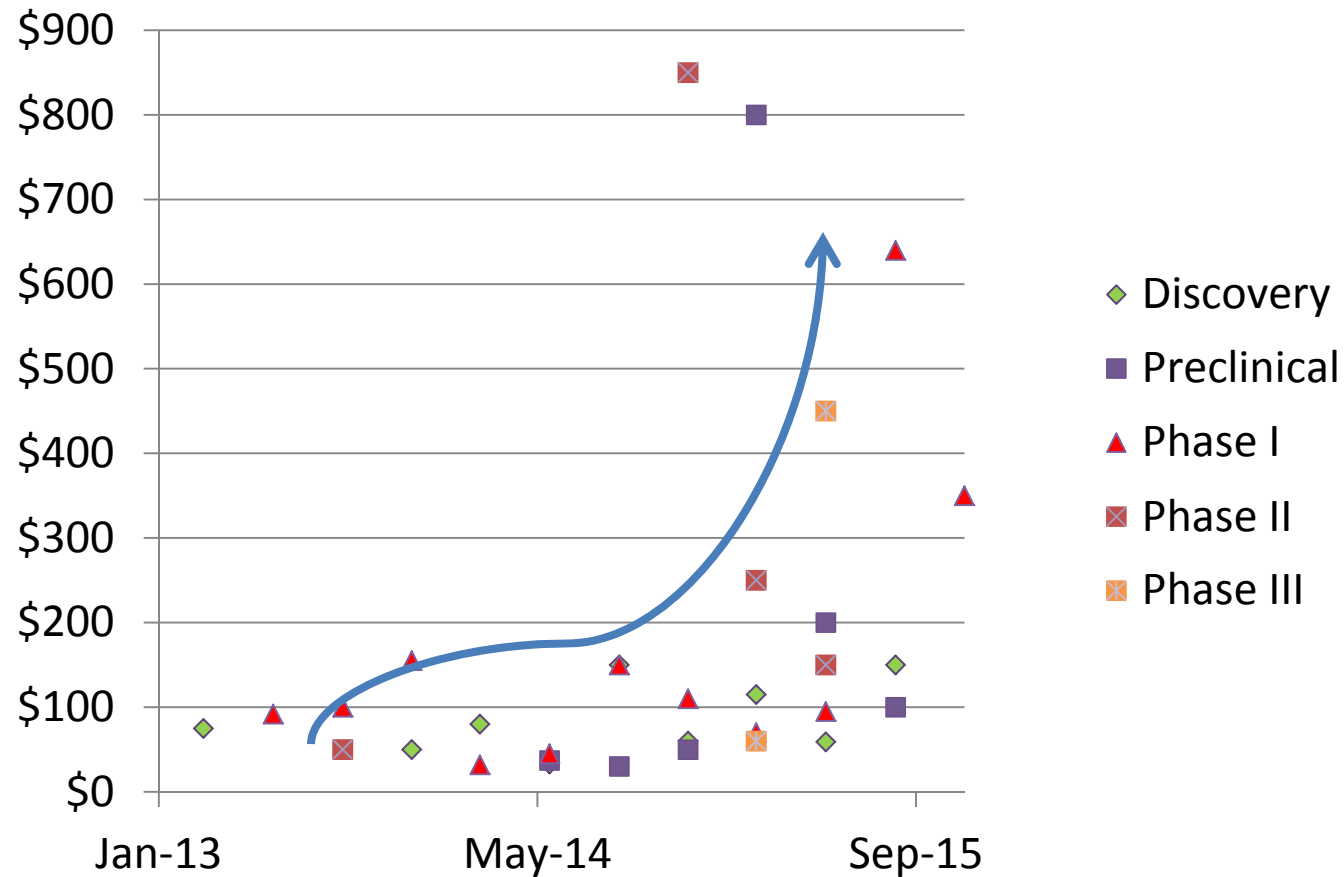
26 Non-Exclusive Combination Clinical Trials were Announced for Immuno-Oncology Compounds so Far this Year

- | | |
|---|---|
| 1 BMS & Lilly <i>Opdivo</i> + Galunisertib | 15 Incyte & Immunovaccine IDO1 + DPX-Survivac |
| 2 Merck & Lilly <i>Keytruda</i> + Pembrolizumab | 16 Lilly & Immunocore Galunisertib + IMCgp100 |
| 3 Incyte & Advaxis IDO1 + ADXS11 | 17 Roche & Amgen MPDL3280 + Talimogene |
| 4 Merck & Eisai <i>Keytruda</i> + Lenvatinib | 18 BMS & Kyowa <i>Opdivo</i> + Mogamulizumab |
| 5 Roche & Celldex MPDL3280 + Varlilumab | 19 MEDI & Mirati MEDI4736 + Mocetinostat |
| 6 Merck & Syndax <i>Keytruda</i> + Entinostat | 20 Merck & Immune Design <i>Keytruda</i> + G100 |



- | | |
|---|--|
| 7 MEDI & Immunocore MEDI4736 + IMCgp100 | 21 GNE & Clovis MPDL3280 + Rociletinib |
| 8 Merck & TetraLogic <i>Keytruda</i> + Birinapant | 22 Merck & MD Anderson <i>Keytruda</i> + Other |
| 9 MEDI & Juno MEDI4736 + CD19 CAR T | 23 MEDI & Advaxis MEDI4736 + Filolisbac |
| 10 Merck & Plexxikon <i>Keytruda</i> + PLX3397 | 24 AZ & Peregrine MEDI4736 + Bavituximab |
| 11 Merck & Amgen <i>Keytruda</i> + Talimogene | 25 GNE & Syndax MPDL3280 + Entinostat |
| 12 Lilly & AZ <i>Cyramza</i> & MEDI4736 | 26 Incyte & Aduro IDO1 + CRS-207 |
| 13 Merck & Tesaro <i>Keytruda</i> + Niraparib | |
| 14 Merck & Dynavax <i>Keytruda</i> + SD-101 | |

Upfront Payments in Immuno-Oncology Deals (\$M)



10 Year Discovery Collaboration to Combine Immuno-Oncology with Cell Therapy

Oncology and Cell Therapy Programs for Autoimmune Diseases Ex-NA (6/15)

Juno

Celgene

- \$150M Upfront Payment
- \$850M in equity, with contingent right to purchase 30% of Juno's OS shares
- \$100M option exercise payment for CD19 and CD22 Programs*
- Joint Programs have 30/70 co-dev cost sharing

Juno has option to co-promote certain Celgene development compounds targeting T cells in US & Major EU

30% PS to Juno on Joint Programs

Celgene has ROW rights to Juno Programs, with PS option on two Programs

* Mid-Teen Royalties for CD-19 and CD-22 Programs

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Preclinical Cancer Immunotherapeutic From Cyclic Dinucleotide Targeting of the STING Receptor

ADU-S100 Receptor Agonist for Cancer Treatment & Vaccine (3/15)

Aduro

Novartis

- \$200M license payment
- \$250M in development milestones
- \$250M in regulatory milestones

Aduro pays 38% of
Worldwide
Development
Expenses

50/50 PS in US
& 45/55 PS for
Major EU &
Japan*

Novartis pays 62%
of Worldwide
Development
Expenses

* Commercialization Expenses Shared in
Same Proportion as Shared Profits

BIOSCI
ADVISORS

Phase I CSF1R Antibody in Combination with Opdivo for Immuno-Oncology Indications

Colony Stimulating Factor 1 Receptor Ab (10/15)

Five Prime

- \$350M Upfront
- \$505M dev & reg milestone payments per Opdivo combo for oncology
- \$542.5M dev & reg milestone payments per other combo for oncology
- \$340M dev & reg milestone payments for non-oncology or synovitis (PVNS)

Bristol-Myers
Squibb

Five Prime has US
co-promotion rights &
option to develop
FPA008 with Five
Prime's internal
pipeline & PVNS

High Teens to
Low Twenties
Royalties & Add'l
if Co-Promote

BMS will evaluate
FPA008 with Opdivo in
six tumor types; BMS
will reimburse 125% of
Independent Dev
Costs if approved in
US, EU or Japan

Replaces 11/14 non-exclusive clinical
collaboration (\$30M upfront & study costs)

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Riding the PD-1 Checkpoint Inhibitor Express: A Global Co-Development Alliance for a Phase II MAb

IPH2201 Humanized NKG2A Antibody as Mono & Combo
Immune Checkpoint Inhibitor (4/15)

Innate
Pharma

MedImmune

- \$250M Upfront Payment
- \$100M in development milestones
- \$925M in regulatory & sales milestones
- CON % share of co-development costs borne by each party

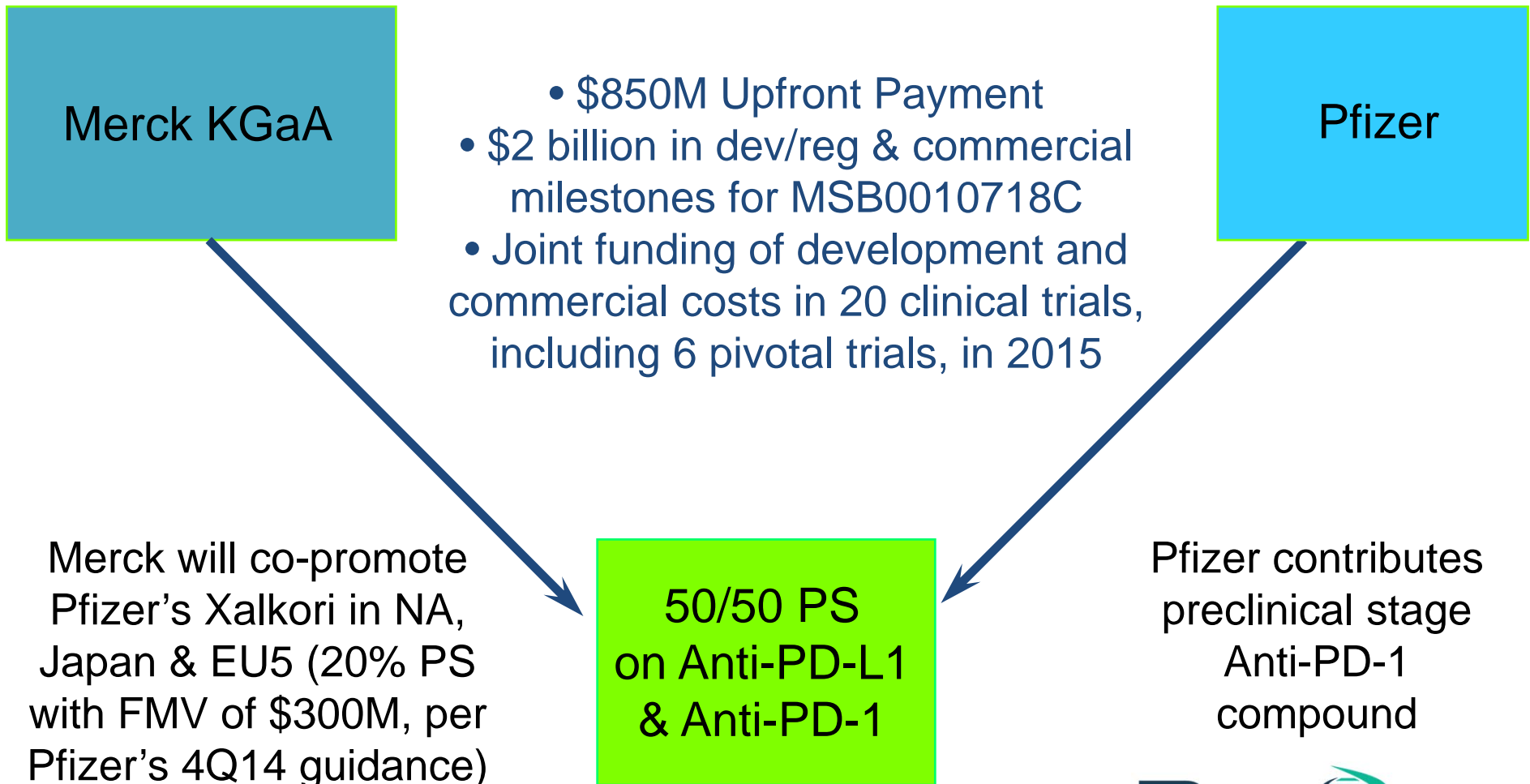
Innate has right to co-promote in Europe for 50% profit split

Double-Digit
Royalties

MedImmune and AstraZeneca book all sales

Sharing of Phase II Immuno-Oncology Compound for Accelerated Development, Cash & a Quid

Anti-PD-L1 Global Strategic Alliance (11/14)



What's Next – Harbingers of Deals to Come

- Biomarkers in Clinical Assessment & as Companion Diagnostics
 - Roche's \$1 Billion Commitment to Biomarkers
 - Biodesix/AVEO Inverts the Dx/Rx Relationship
 - Is There a Coming Era of “Companion Therapeutics”?

Roche/Foundation Medicine (1/15) Looks to Redefine the Field

TRANSFORMING ONCOLOGY

FMI'S STRATEGIC COLLABORATION WITH ROCHE

- Focuses on improving patient care in oncology
 - The strategic collaboration aims to further advance FMI's leading molecular information platform while providing Roche with the opportunity to identify and develop novel treatment options for patients
- Enhances molecular information business and R&D capabilities
 - 5-year commitment to broad utilization of FMI molecular information platform for Roche pipeline assets
 - New product development collaborations: ctDNA, cancer immunotherapy, companion diagnostics
- Expands commercialization efforts
 - Enhanced market development efforts in U.S. through Genentech resources
 - Acceleration of global access through Roche's ex-U.S. commercial infrastructure
- Results in Roche acquiring majority interest in FMI
 - Roche to acquire majority interest in FMI up to 56.3% on a fully diluted basis through a tender (aggregate value of ~\$780 million) and acquisition of newly issued shares
- Strengthens FMI's balance sheet and supports investment opportunities
 - Includes primary capital investment of \$250 million in FMI at \$50 per share
 - >\$150 million in additional payments and milestones over 5 years from R&D collaboration
 - Additional cash and in-kind support from commercialization activities
- Maintains independent innovation
 - FMI retains operating independence and current management team while leveraging Roche's expertise and breadth of experience in precision medicine and oncology

A Dx Leading the Phase II Trial of a Lung Cancer Compound

Biodesix Partnership: April 2014



AVEO and Biodesix Partner to Co-Develop and Commercialize Ficlatusumab with a Companion Diagnostic

- Unique collaboration where the diagnostic company provides funding for POC clinical development in NSCLC
 - Biodesix will fund up to \$15 million of the cost of the confirmatory phase 2 study in NSCLC and all companion diagnostic development costs
 - 50/50 sharing of ficlatuzumab development and commercialization expenses beyond confirmatory phase 2
 - 50/50 sharing of potential profits from ficlatuzumab
 - Biodesix retains revenue from companion diagnostic
 - AVEO to lead worldwide commercialization of ficlatuzumab
- Agreement advances ficlatuzumab with external funding while retaining significant downstream value for AVEO

Is the Era of “Companion Therapeutics” Just Ahead?

“When the IVD-origin knowledge integrator amasses enough data and understanding to guide therapy decisions in large categories, particularly drug choices, it will become more valuable than any of the drug suppliers.”

“When Illumina Buys Roche: The Dawning of the Era of Diagnostic Dominance” In Vivo, 2014

- Robert Easton (formerly Wilkerson Group) & Alain Gilbert (formerly Abbott Diagnostics)

What's Next – Harbingers of Deals to Come

- Biomarkers in Clinical Assessment & as Companion Diagnostics
- Therapy for Orphan and Underserved Conditions
 - 95% of 6,000+ rare diseases w/ no approved therapy
 - 140 compounds/yr designated as orphan by FDA
 - 17 of 41 NMEs approved in 2014 were Orphan Drugs
 - Challenges include models of phenotype, trial recruitment, big data, manufacturing costs
 - Approaches include gene therapy/editing & cell therapy

Gene Therapies for Orphan Diseases of the Retina

XLRS, XLRP & AAV Gene Therapy Platform for Ophthalmology (7/15)

AGTC

- \$94M upfront payment
- \$30M equity investment
- \$472.5M in milestones for XLRS & XLRP
- \$592.5M in milestones across all discovery programs

Biogen

AGTC has co-dev option for Initial Program for 50/50 PS, plus US co-promotion rights for second

XLRS has Low Double-digit to Mid-Teen Royalties

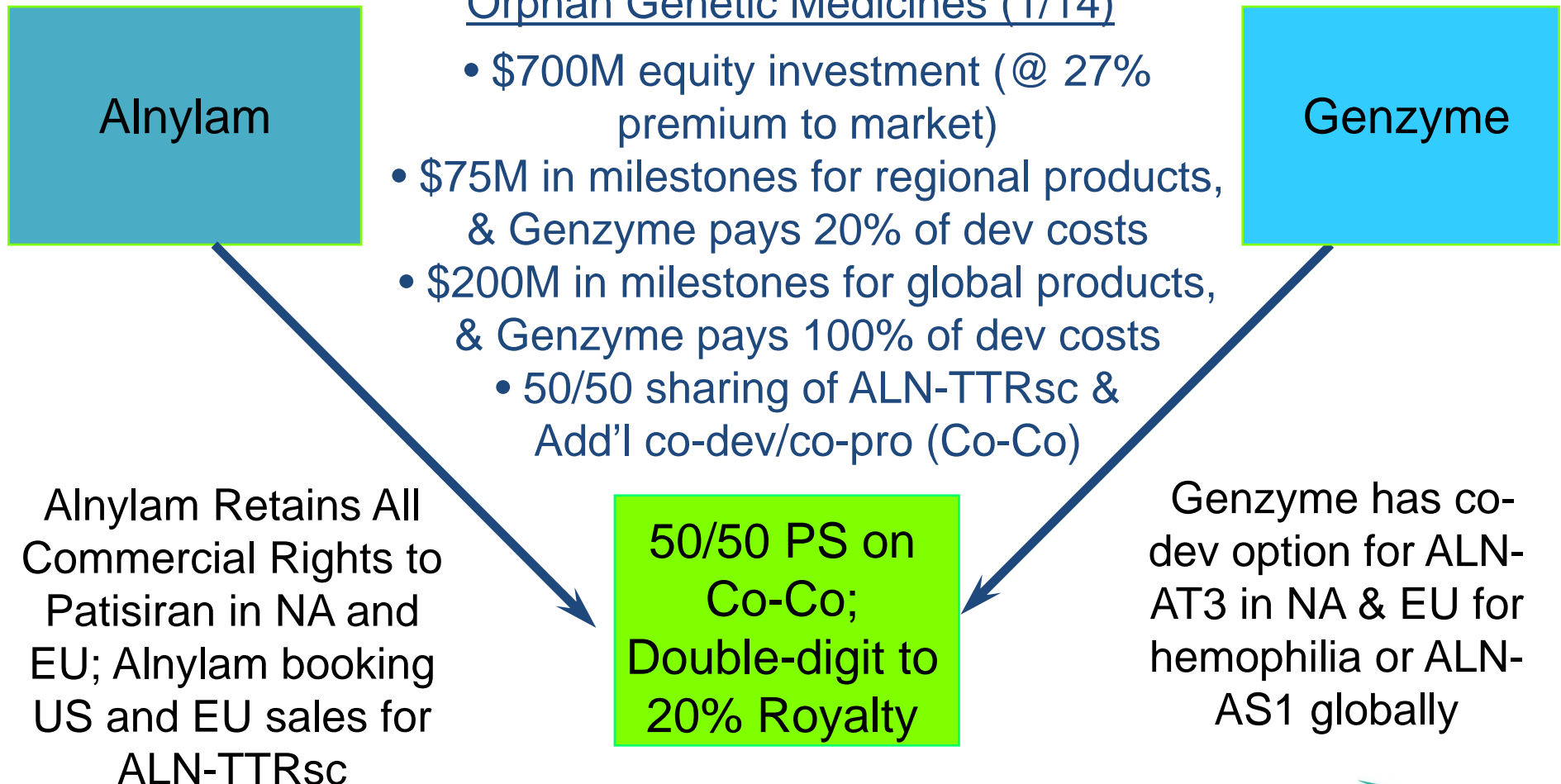
Biogen pays dev costs of next clinicals; options for two eye & one non-eye gene therapies

X-linked Retinoschisis (XLRS)
X-linked Retinitis Pigmentosa (XLRP)

BIOSCI
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Phase III, Phase II Orphan Compounds, with More to follow: Broadening A Collaboration to Go Regional & Global*

Patisiran, ALN-TTRsc and RNAi Therapeutics for Orphan Genetic Medicines (1/14)



* Parties formed 2012 alliance for Japan & Asian rights to ALN-TTRsc

What's Next – Harbingers of Deals to Come

- Biomarkers in Clinical Assessment & as Companion Diagnostics
- Therapy for Orphan and Underserved Conditions
- Biosimilars As the Pressure Relief Valve for Drug Costs
 - EU has led with 20+ approvals to date & 20-30% price discounts
 - Almost \$70B worth of 1st gen MAbs & fusion proteins have patents expiring by 2020
 - Biosimilars have \$18 Billion in sales potential by 2022

Phase 2a Lucentis Biosimilar Commands Premium Payments

PF582 (ranibizumab) for Retinal Disease & VEGF Therapeutic Segment (2/15)

Pfenex

- \$51M upfront payment
- \$31M in dev/reg milestone payments
 - \$260M in sales milestones
 - Shared costs of Phase III

Hospira

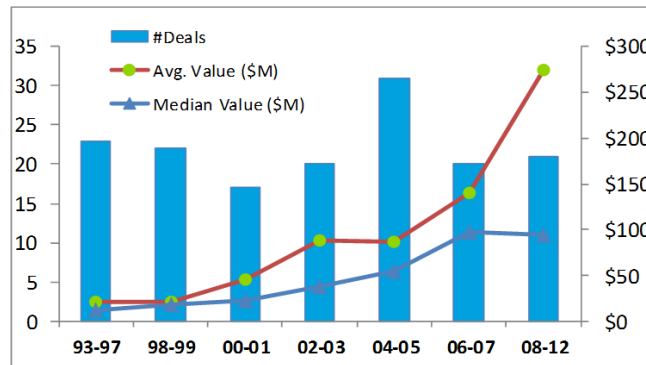
Tiered
Double-digit
Royalties

**This Presentation is Available on our Discussion Website,
BioSciBD.com**

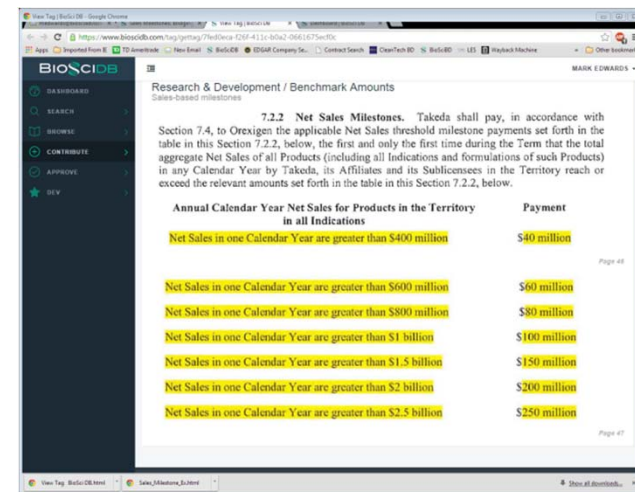


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