



# Commercial Deal Structures & Recent Trends

*European Association of Pharma Biotechnology*

Christi Mitchell

March 7<sup>th</sup> 2016

medius  
associates

# Deal Watch



Based on Medius monthly review of pharma deals which captures the top deals by public headline value plus other deals of note. We include deals in the month of announcement and typically update on closure.

## HEADLINE VALUES

As frequently quoted in press releases, based on the sum of initial [upfront / signature] payments, option fees, R&D funding, development milestone payments, sales threshold and other success or contingent payments, as cash or equity. This does not typically include royalty payments.



## 2015 Overview

# 2015 Acquisitions

Values US \$bn	2013	2014	2015
DW top 20 acquisitions	159.7	296.3	276.6

The 2015 deal news landscape showed:

- Tax inversion still impacting deals; companies not being deterred e.g. Pfizer, Shire
- A few major asset swaps; e.g. Sanofi and Boehringer Ingelheim
- Pressure on for demergers; e.g. GSK, Sanofi
- The pricing debate ramping up
  - Gilead under increasing pressure on its US price
  - Turing Pharma / Valeant under investigation for putting profits before patients



# Company acquisitions

2015		\$bn
Allergan	Pfizer	160,0
Pharmacyclics	AbbVie	21,0
Hospira	Pfizer	17,0
Salix	Valeant	14,5
Synageva BioPharma	Alexion	8,4
Par	Endo	8,0
Receptos	Celgene	7,2
Dyax	Shire	6,5
NPS	Shire	5,2
Acerta Pharma	AstraZeneca	4,0
Auspex	Teva	3,5
Amdipharm Mercury	Concordia	3,5
BI Roxane	Hikma	2,7
ZS Pharma	AstraZeneca	2,7
Ikaria	Mallinckrodt	2,3
RIMSA	Teva	2,3
Kythera	Allergan	2,1
Cardioxyl	BMS	2,0
Cordis [J&J]	Cardinal Health	1,9
Dezima Pharma	Amgen	1,5
		<b>276.6</b>

2014		\$bn
Allergan	Actavis	66,0
Covidien	Medtronic	42,9
Forest	Actavis	25,0
Sigma-Aldrich	Merck KGaA	17,0
GSK	Novartis	15,5
Alliance Boots	Walgreen	15,3
Life Technologies	Thermo Fisher Scientific	15,0
Merck & Co	Bayer	14,2
Biomet Inc	Zimmer	13,3
Becton Dickinson	CareFusion	12,2
Cubist	Merck & Co	9,5
Intermune	Roche	8,3
Novartis	GSK	7,1
Covance	Labcorp	6,0
Questcor	Mallinckrodt	5,6
Novartis	Eli Lilly	5,4
Abbott	Mylan	5,3
Omega Pharma	Perrigo	4,5
Galderma	Nestle	4,2
J&J	The Carlyle Group	4,0
		<b>296.3</b>

# Licensing deals

Values US \$bn	2013	2014	2015
DW top 20 licensing deals	18.2	27.5	28.8

- The values for the top licensing deals were slightly up on 2014
- Upfront payments were fairly variable;
  - range from 1% - 35% of the headline value in the top DW deals
- As in 2014; the top deals brought in significant upfronts,
  - 5 top 20 deals had upfront payments >18% of the headline value
- Early stage deals were capturing big headlines
  - 8 of the top 20 deals were for platform/discovery collaborations
- Notably very deal active companies: AstraZeneca, Sanofi



# Licensing deals

2015		\$bn
Hanmi	Sanofi	4.2
Regeneron	Sanofi	2.1
Galapagos	Gilead Sciences	2.0
Xencor	Amgen	1.7
Five Prime Therapeutics	BMS	1.7
Lexicon	Sanofi	1.7
BioNTech	Sanofi	1.5
Innate	AZ	1.2
Arcturus Therapeutics	Ultragenyx	1.2
Halozyne Therapeutics	AbbVie	1.2
Parion Sciences	Vertex	1.1
Achillion	J&J	1.1
AGTC	Biogen	1.0
Esteve	Mundipharma	1.0
Juno Therapeutics	Celgene	1.0
BioAtla	Pfizer, Inc.	1.0
Intrexon	Merck KGaA	0.9
Hanmi	Janssen	0.9
Voyager Therapeutics	Sanofi (Genzyme)	0.8
Isis	Janssen Biotech	0.8
		<b>28.8</b>

2014		\$bn
Edison	Dainippon	4.2
Merck KGaA	Pfizer	2.8
Ablynx	Merck & Co	2.3
Bayer	Merck & Co	2.1
Macrogenics	Takeda	1.6
Nogra Pharma	Celgene	1.5
Proteostasis	Astellas	1.2
NewLink Genetics	Genentech Roche	1.1
Intacia	Sevier	1.0
Ophthotech	Novartis	1.0
Sutro Biopharma	Celgene	1.0
Merrimack	Baxter	0.9
Geron	Janssen Biotech	0.9
MannKind/ Sanofi	Sanofi	0.9
Cellectis	Servier	0.8
Aduro BioTech	J & J	0.8
Infinity	AbbVie	0.8
Alnylam	Genzyme	0.7
Macrogenics	J&J	0.7
Cytokinetics	Astellas	0.6
		<b>27.5</b>

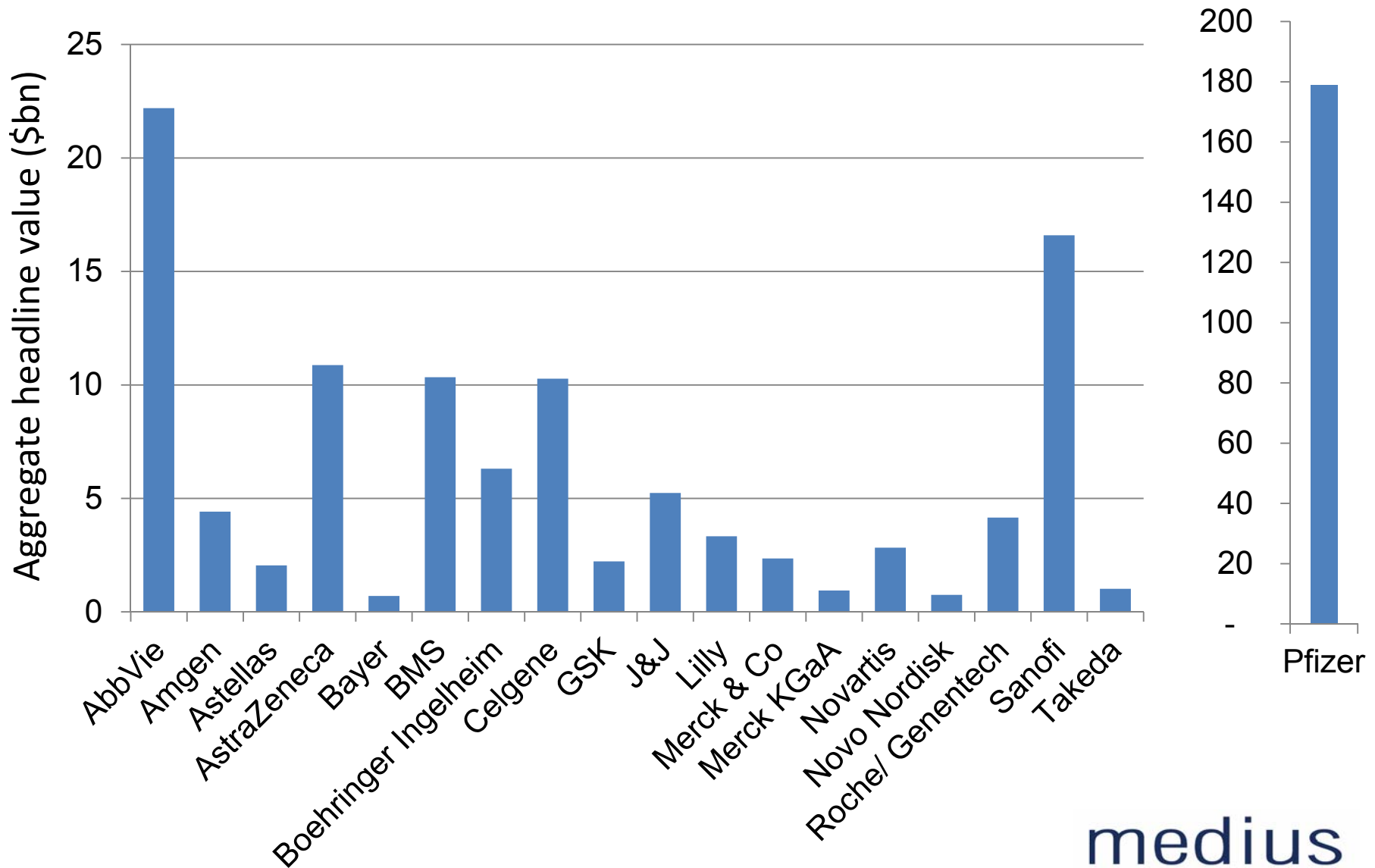
# Who did what in 2015?



All values in \$



# Large pharma inward deal spend in 2015

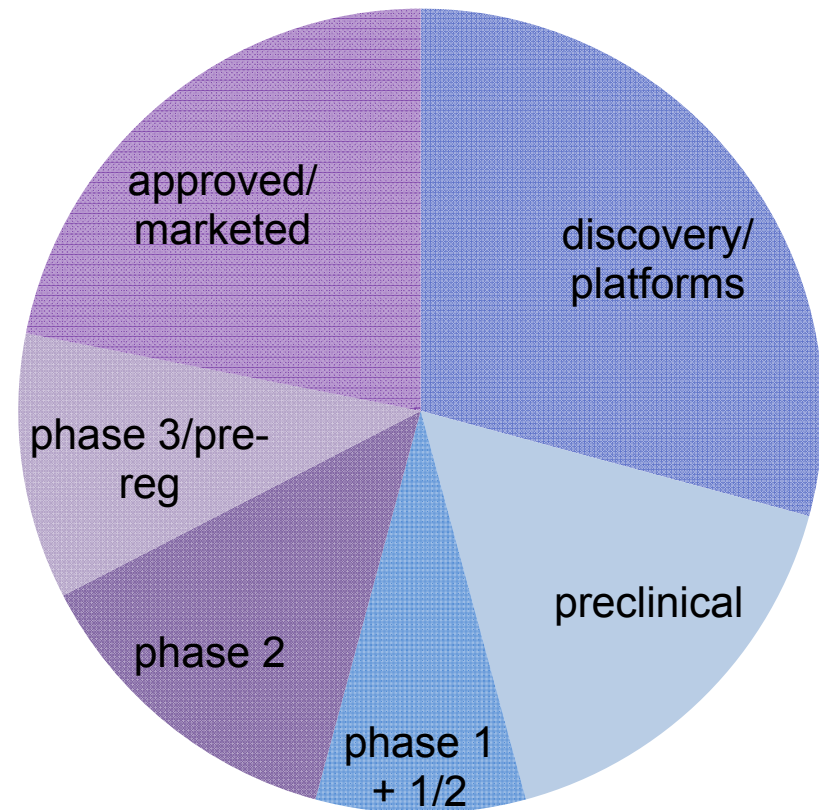




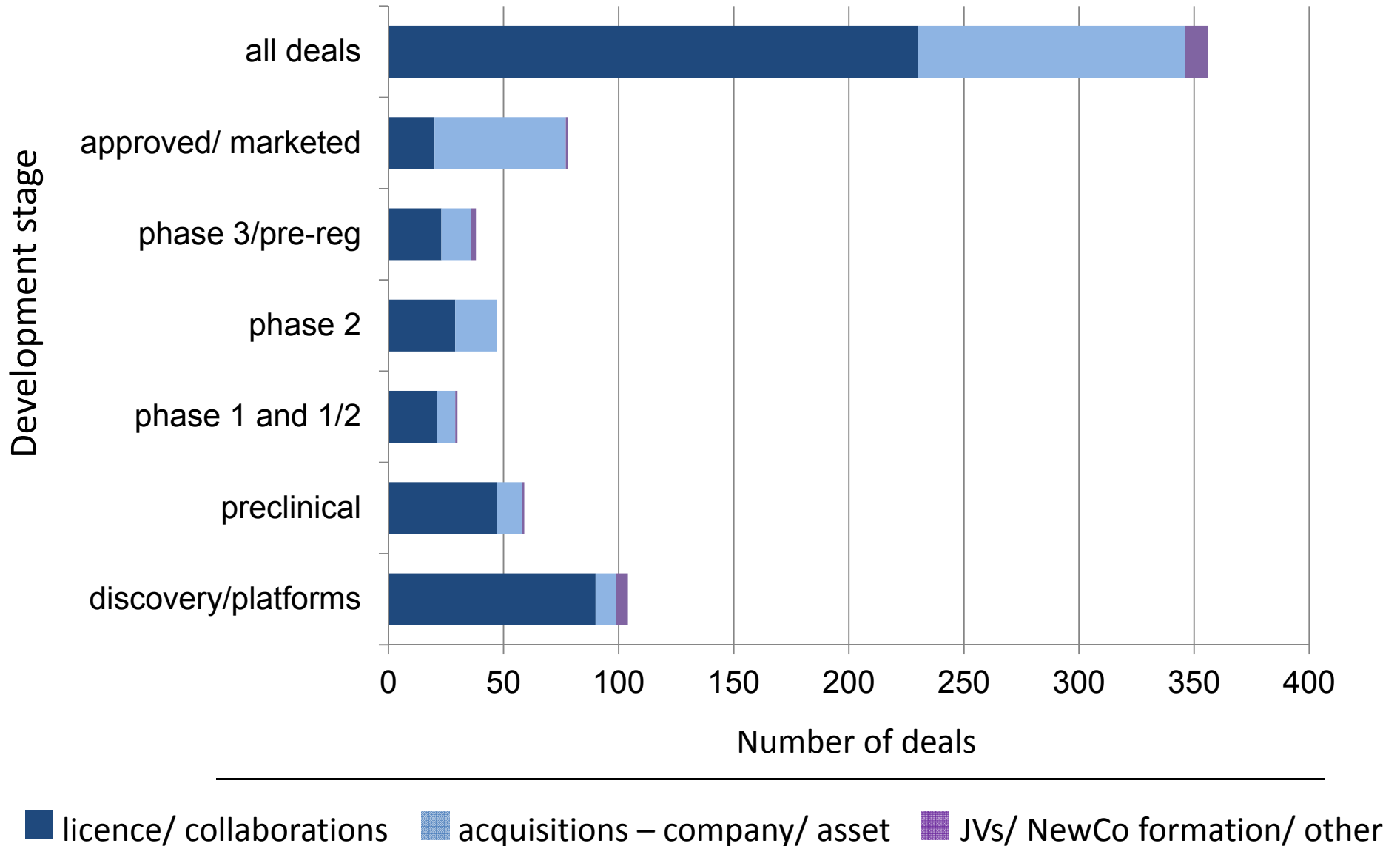
## Deal trends

# Deals by development stage

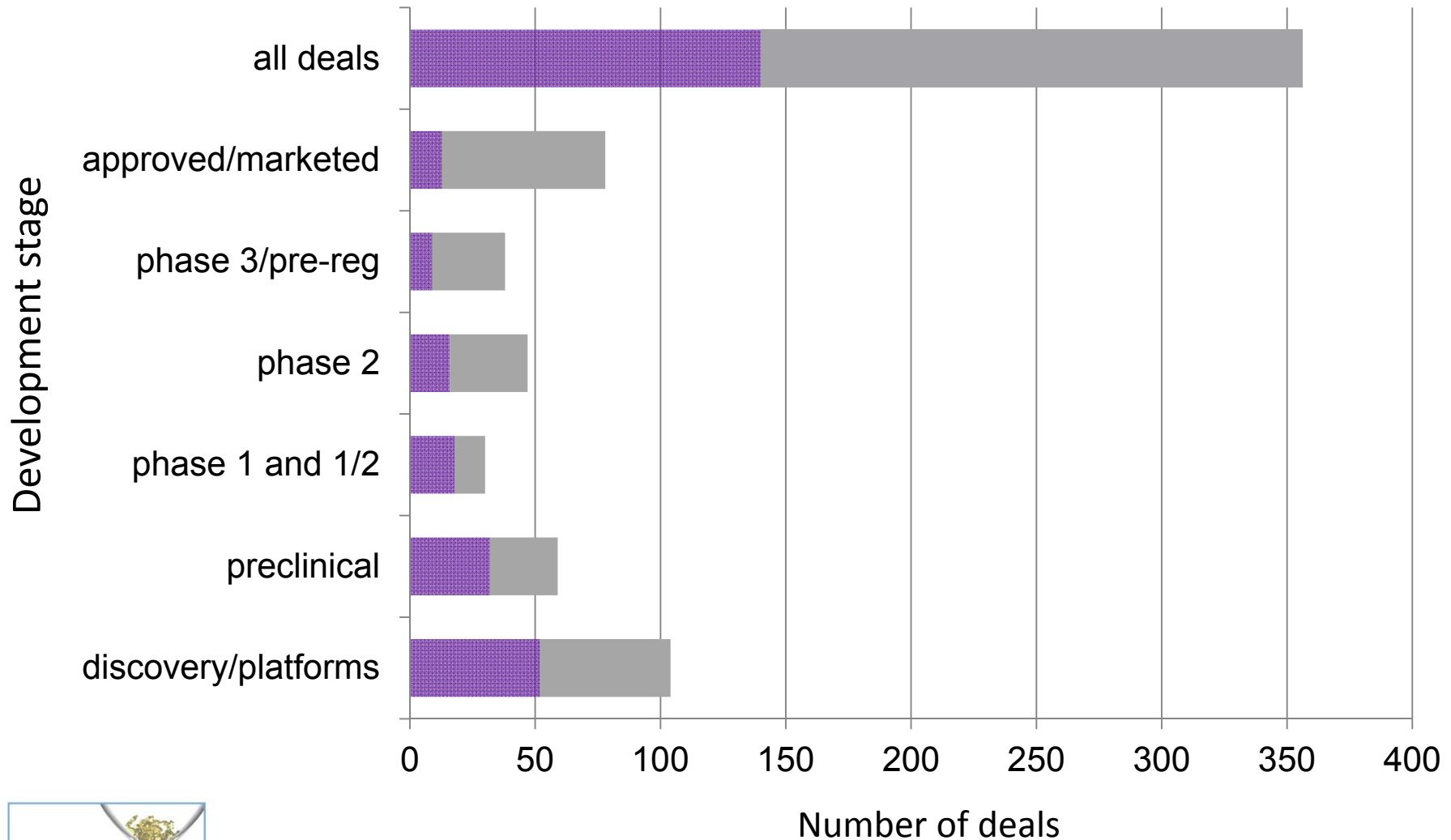
- Analysis focuses on pharma acquisitions and licensing deals for proprietary assets with financials disclosed (356 deals)
- Overall more deals done at non-clinical versus clinical stages
- Proportion of clinical stage deals similar to 2014
- Significant shift towards early stage discovery/ platform deals cf 2014
- Risk management influences deal type



# Type of deal by development stage – all deals



# Large pharma deal activity by development stage



■ large pharma    ■ other companies

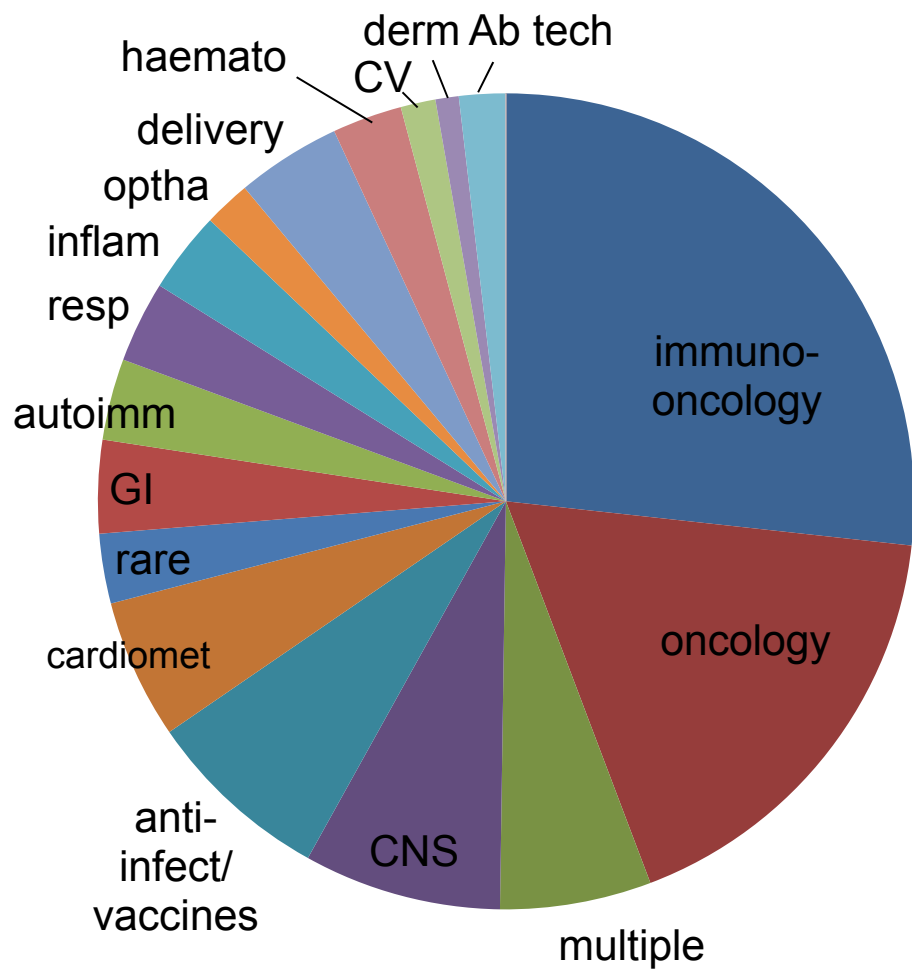
medius  
associates



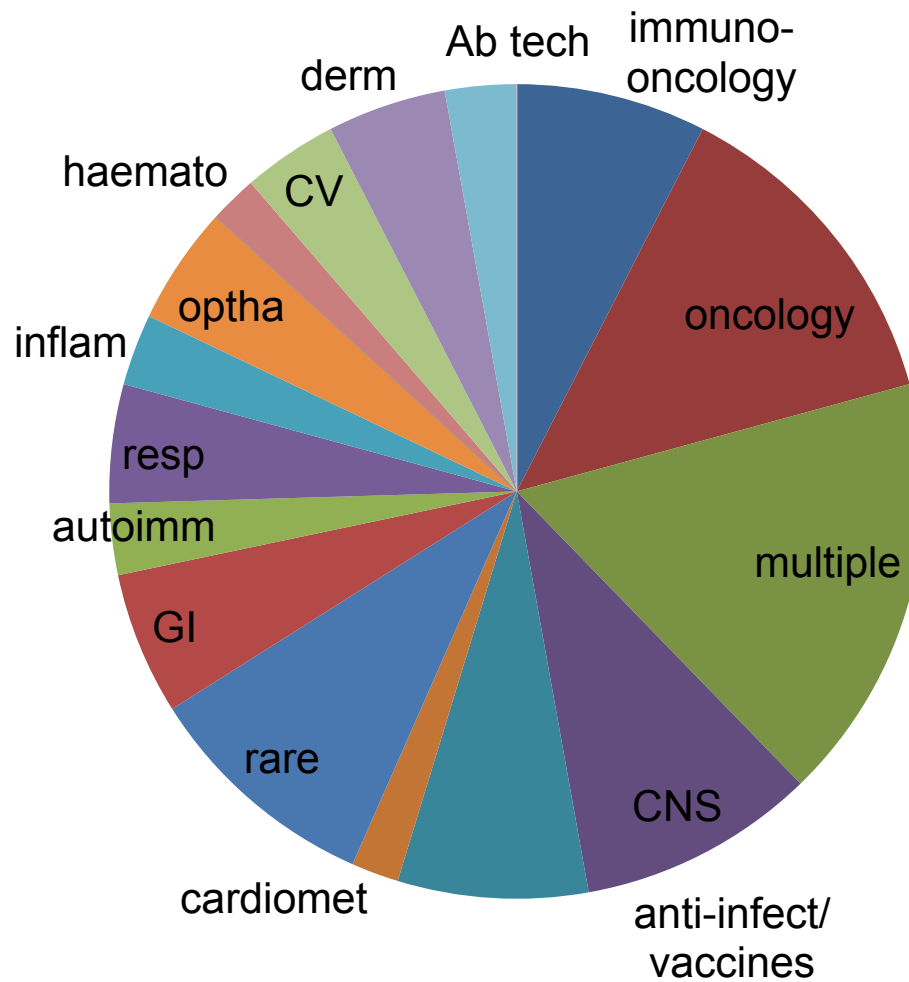
Therapeutic areas

# Top therapeutic areas – all development stages

## Top TAs for licensing

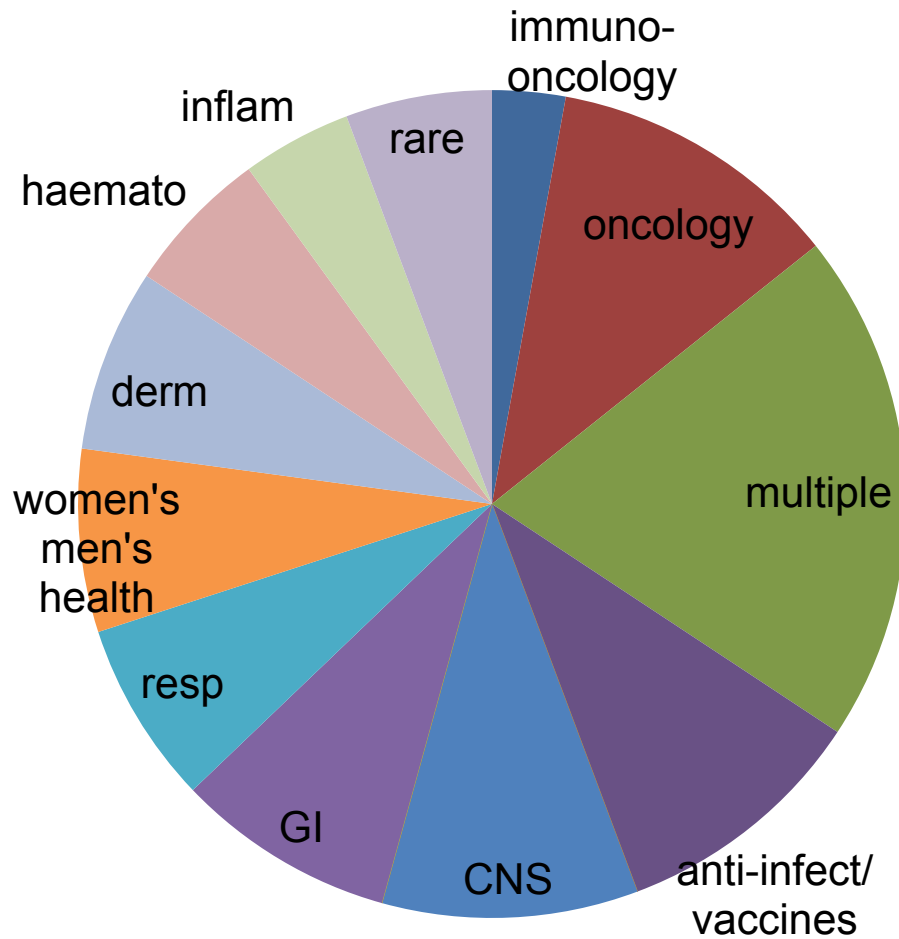


## Top TAs for acquisition

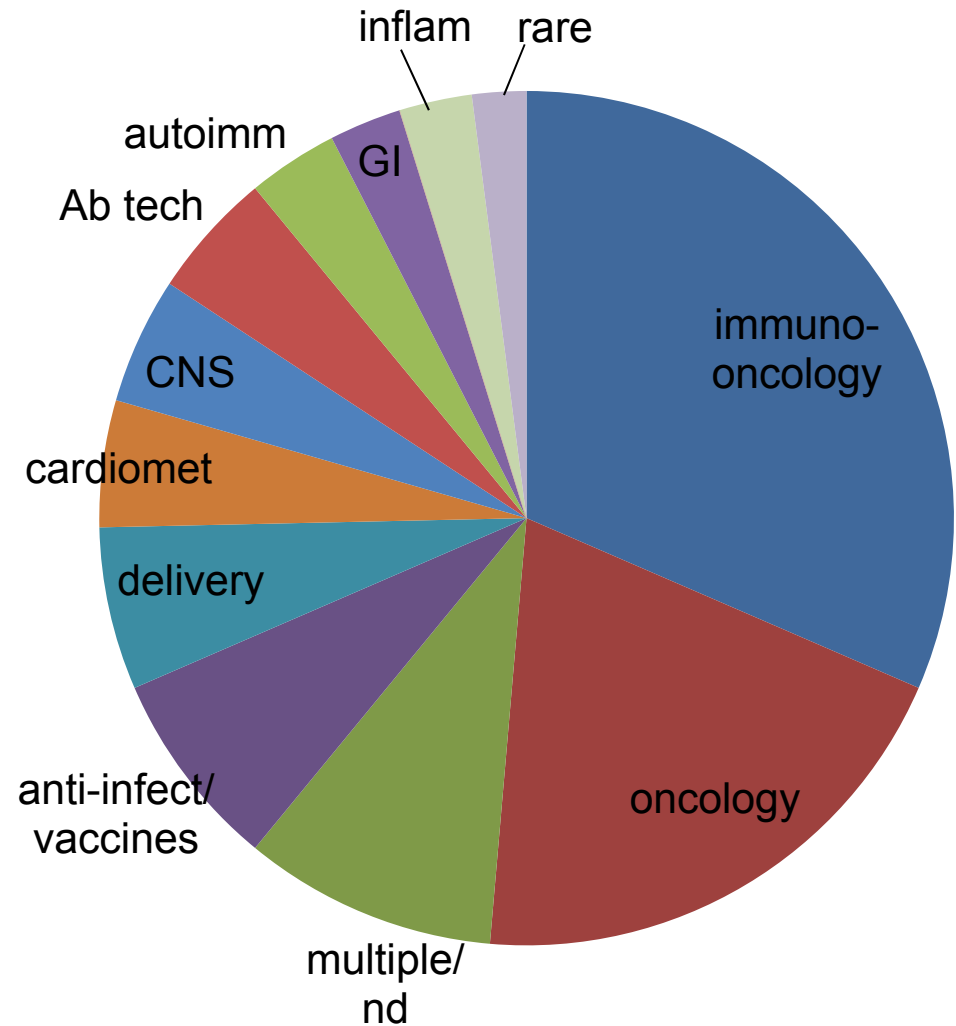


# Top TAs based on development stage

## Market/approved stage

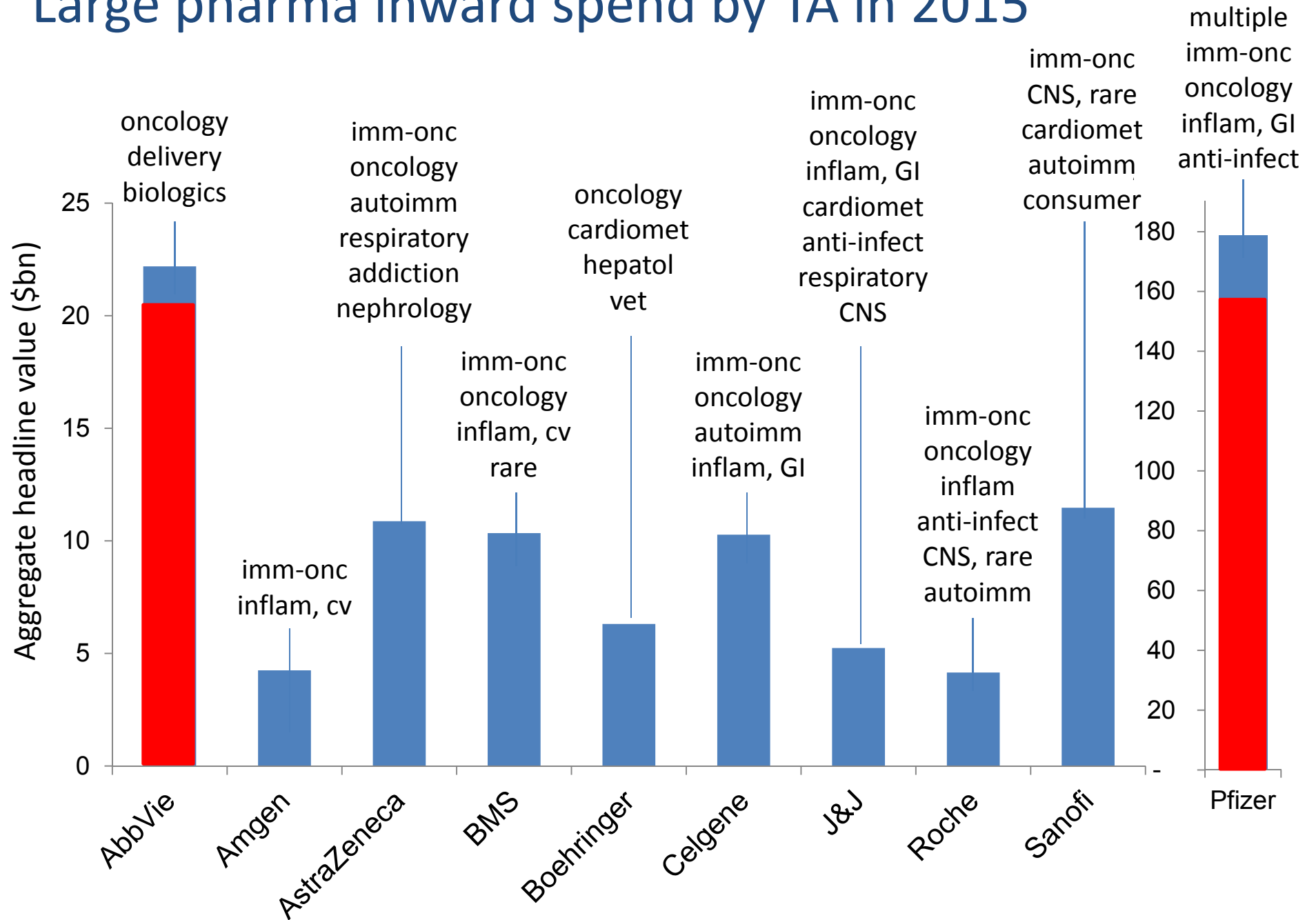


## Non-clinical deals





# Large pharma inward spend by TA in 2015

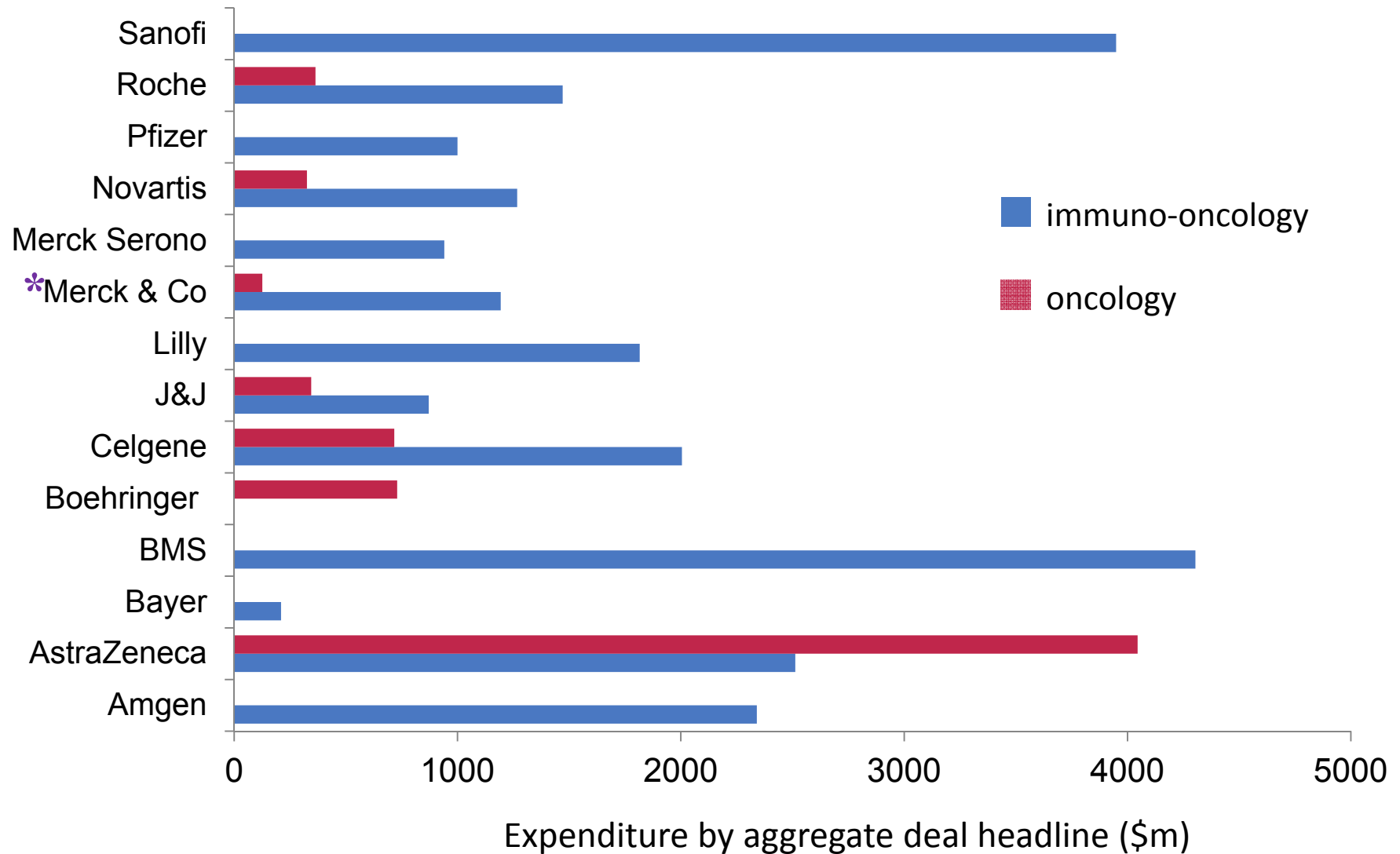


# Analysis of immuno-oncology deals

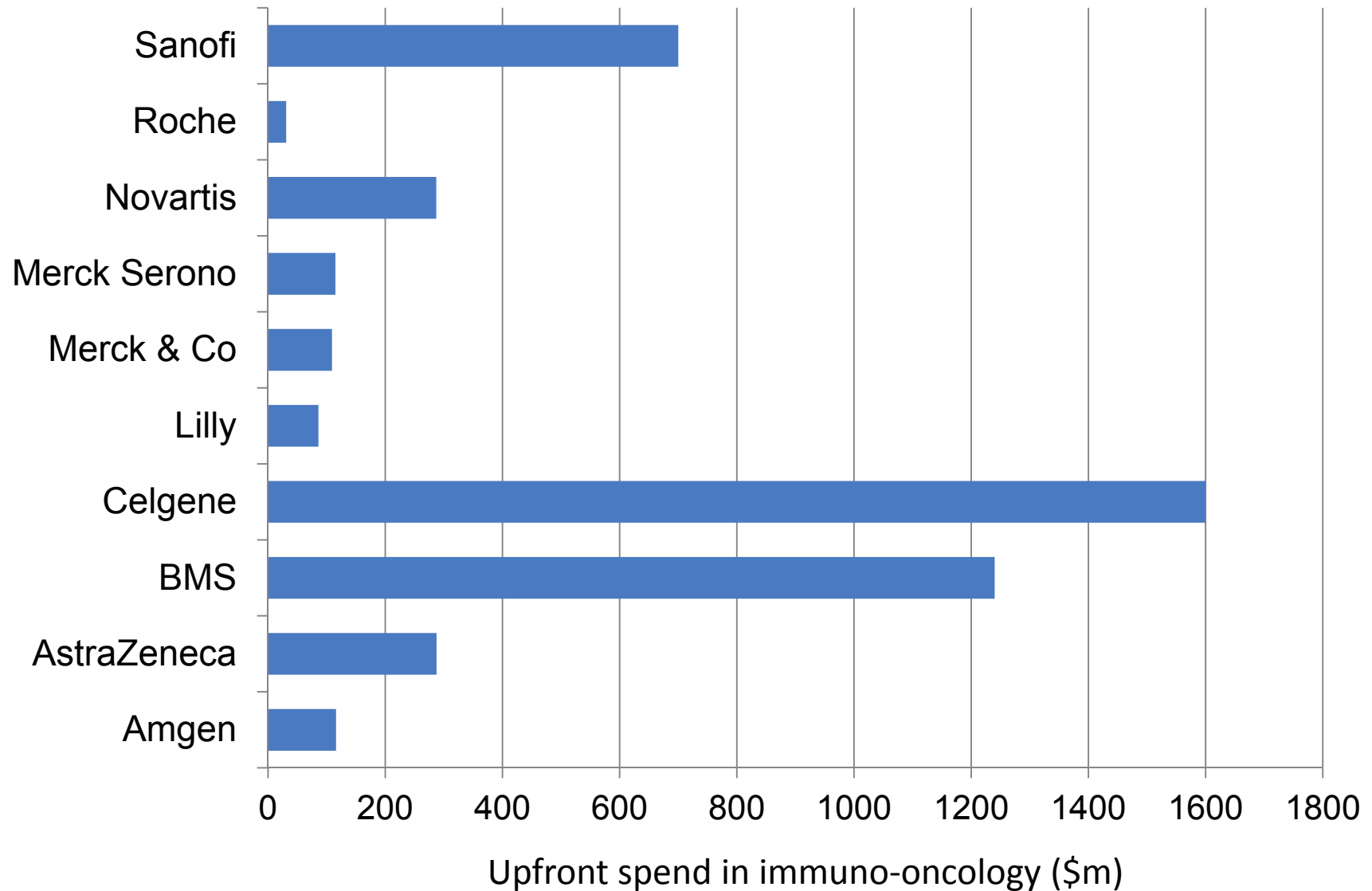
- During 2015 we reviewed 67 transactions focused on immuno-oncology; 46 were at non-clinical stage
- 58 were licensing-based deals
- Also numerous clinical collaborations to assess combinations of immuno-oncology/ oncology therapies for specific cancer types
- Merck & Co particularly active in clinical collaborations for its anti-PD-1 antibody (Keytruda) with Amgen, Lilly, GSK etc
- BMS and Sanofi the largest spenders in immuno-oncology in headline values
- However Merck & Co could pay over \$4.6bn in total milestones if all 12 targets in Ablynx expanded collaboration achieve all milestones
- Celgene and BMS largest spend upfront based on disclosed financial terms

# Total headline spend - oncology vs immuno-oncology

- Excludes AbbVie \$22bn acquisition of Pharmacyclics

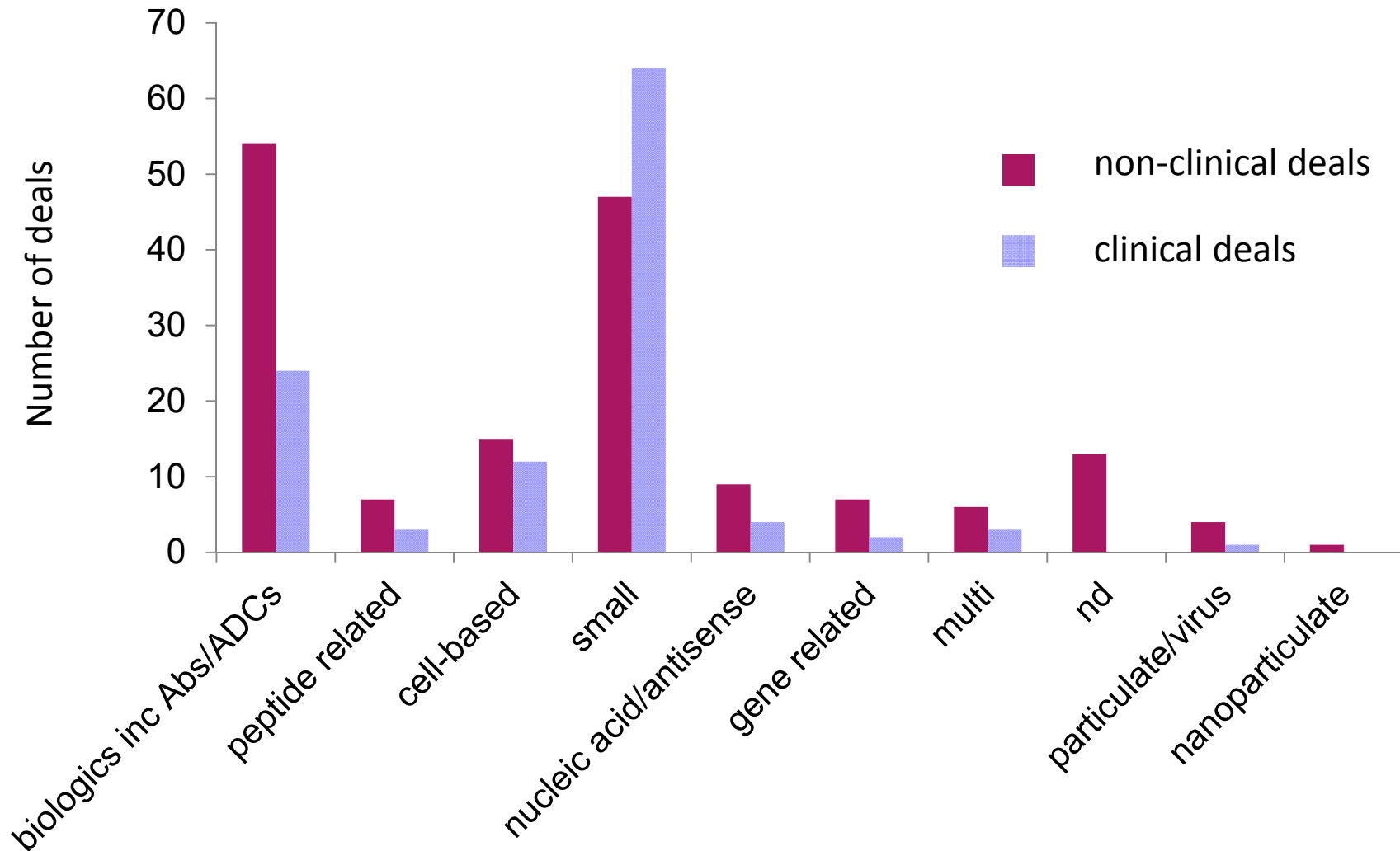


# Total upfront spend in immuno-oncology



# Therapeutic entities – trends

- All types of therapeutic entities represented in deals across various stages but small molecules dominated phase 2 and 3 deals



# Selected gene therapy deals

Companies	Product/ Technology	Financials \$m
uniQure/ BMS	multiple targets in cv diseases inc S100A1* programme for congestive heart failure; up to 10 targets using uniQure’s AAV** platform (pc)	2,307 (100 near term inc 50 upfront, 32 equity, 15 for selection of 3 targets, ms + further equity)
enGene/ Janssen	“Gene Pill” and enema non-viral gene delivery; option to license lead product candidate, EG-12, for gut-localised expression of IL-10 for inflammatory bowel disease (pc)	339
AGTC/ Biogen	X-Linked Retinoschisis and X-linked Retinitis Pigmentosa AAV programmes + options to 3 other programmes (p1)	1,065 (uf 124 inc 30 equity)
Voyager Therapeutics/ Sanofi (Genzyme)	multiple CNS AAV programmes, inc Parkinson’s disease, Friedreich’s ataxia and Huntington’s disease, and other CNS disorders; ex US with US profit share (p1)	845 (uf 100 in 65 cash, 30 equity + in-kind contributions)

\*calcium sensor and master regulator of heart function; \*\* adeno-associated virus

# CRISPR/Cas-9 gene editing

- RNA-guided gene editing
  - utilises Cas-9 (bacterially derived protein) and synthetic guide RNA to introduce a double strand break in the DNA at a specific site
- Can add to, disrupt or change the sequence of specific genes
- Enabling approach to directly modify or correct defective genes with the potential for curative therapies
- Focus on somatic (non-germline) cells
- Two approaches to therapeutics:
  - *in vivo* where delivery is established e.g. liver, eye, lung
  - *ex vivo* e.g. haemoglobinopathies, certain types of immunodeficiencies, specific immuno-oncology therapies
- CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Caribou Biosciences have certain rights to CRISPR/Cas-9 IP

CRISPR = clustered regularly interspaced short palindromic repeat

# CRISPR/Cas-9 gene editing deals

Companies	Product/ Technology	Financials \$m
CRISPR Therapeutics/ Vertex	4-yr collaboration using CRISPR/Cas-9 technology + options to license up to 6 gene-based therapies for CF + haemoglobinopathies	2625 (u/f 105: 30 eq + 75 cash; 420/ prog)
Editas/ Juno	immuno-oncology collaboration - 3 programmes utilising Editas gene editing technologies, inc CRISPR/Cas-9, with Juno's CAR and TCR technologies	737 (uf 25; 230/ prog; 22 R&D funding)
CRISPR Therapeutics/ Bayer	JV to discover, develop therapeutics to cure blood disorders, blindness, and congenital heart disease	335 (uf 35)
Intellia Therapeutics/ Novartis	5-yr collaboration on engineered CAR T cells + ex vivo editing of haematopoietic stem cells; certain rights for in vivo therapeutic uses of CRISPR	nd (increasing equity investment + licence fees + R&D funding)
4 institutions/ AstraZeneca	CRISPR/Cas-9 in cancer drug discovery	nd





# University

## Finance and Valuations

- Recent Notable Collaborations
- Trends
- Conclusions

# University / Industry Collaboration

University	Partners	Aim	Funds
UCLB (University College London)	UCL Technology Fund	technology investment fund: with funding for early stage proof of concept, licensing projects and new spinout companies. includes early stage proof-of-concept funding, development funding to achieve successful licensing outcomes, and funding for spin-out companies to take opportunities through to market.	£50M
Imperial College London University College London University of Cambridge.	The Apollo Therapeutics Fund: unique collaboration between three global pharmaceutical companies (AstraZeneca, GlaxoSmithKline and Johnson & Johnson) and the 3 technology transfer offices (TTOs) responsible for commercialising the research.	The first fund created to pool resources from 3 major pharma companies with 3 leading UK universities. Apollo Therapeutics Fund aims to significantly improve the speed and potential of university research being translated into novel medicines & drive forward therapeutic innovation. The industry partners will also provide R&D expertise and additional resources to assist with the commercial evaluation and development of projects.	£40M (Includes £10M/pharma co over 19 years and £3.3 from each university)

# Cambridge Enterprise

- Cambridge Enterprise
- 2015- lucrative exits as US corporates Janssen and Apple acquired XO1 and VocallQ, respectively – the latter a deal worth up to \$100m. The technology transfer team signed 123 commercial and research licences and filed 159 patent applications.
- £16M seed fund
- 2015, Cambridge Enterprise Seed Funds returned £3.7m to the fund from the sale of shares in three companies.
- **Kings College London**
- King's College London has (Jan 2016) entered into an exclusive license agreement with Pfizer Inc. for the development of a series of adeno-associated virus (AAV) gene therapy vectors. No details disclosed



# Trends

- Figures released by the Higher Education Funding Council for England in 2015 suggest that the worth of university / industry partnerships grew by £300 million to £3.9 billion during 2013-14.
- China and the US dominate the innovation indicators.
- In China, universities receive only 8 per cent of national research funding directly, but they also work closely with government-controlled enterprises that receive the majority of China's R&D funds.
- in the US, universities and their spin-off companies can be commercial players in their own right, thanks to the 1980 Bayh-Dole Act, which gives universities ownership rights over their inventions.
- The Hefce (UK) Higher Education – Business and Community Interaction Survey: 2013-14 suggests that UK universities as a whole outperform those in the US and Japan in terms of their proportion of industry-funded research and income from spin-off equity – yet at the level of individual institutions, the innovation indicators suggest that the UK performs far less well.
- There is still a great need to better manage the industry-university relationship. It appears that pharma and biotech companies are looking for more early stage technology- will this be the catalyst?



# Changing Model

- University/industry collaboration seen as increasingly important to economy
- Industry move towards more early stage/high risk deals
- Are we seeing a move away from straight licensing?
- Encouragement needed for corporates to engage more with universities.
- Recognition of the importance of increasing university impact and connection to the outside commercial world.
- Multi university/industry collaboration with added industry expertise.
- Shift to a needs-driven model that takes much of the luck out of the equation. How? Instead of passively waiting they are proactively working with corporate partners and tech scouts – and with their own researchers --
- Promoting both financial impact and non-financial/social impact on society.
- UK Government looking for university collaboration income - £5bn pa by 2025.





Conclusions

## So what can we expect in 2016?

- Oncology and Cardiovascular (including diabetes) will continue to be the assets attracting the most deals
- Out-licensing early or late (but not in the middle) could be your best choice
- Increasing early stage deals should indicate greater Industry/University collaboration
- Options are becoming an increasingly popular way to manage risk
- Don't despair if your therapeutic area or technology is unfashionable. Its day may yet come!



## So far in 2016:

- Baxalta/Shire: acquisitions for \$32bn; +\$2bn on original offer
- Nestle collaboration with Seres Therapeutics, headline \$1.9bn
- Options, options, options!
- Oncology still hot...
- Majors very active: Merck, Sanofi, Roche, BMS

And thanks to the Deal Watch reporting team!



Jill Ogden



Bridget Lacey



Roger Davies



Catharine Staughton



Partnering



Strategy

Valuation



Due Diligence

Negotiation



Benchmarking



medius  
associates

Deal Watch: Current Trends in Deals

[www.medius-associates.com/deal-watch/](http://www.medius-associates.com/deal-watch/)