

APPLE TREE PARTNERS

Early-Stage Biotech Finance & Valuation

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Sam Hall

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Who Am I?

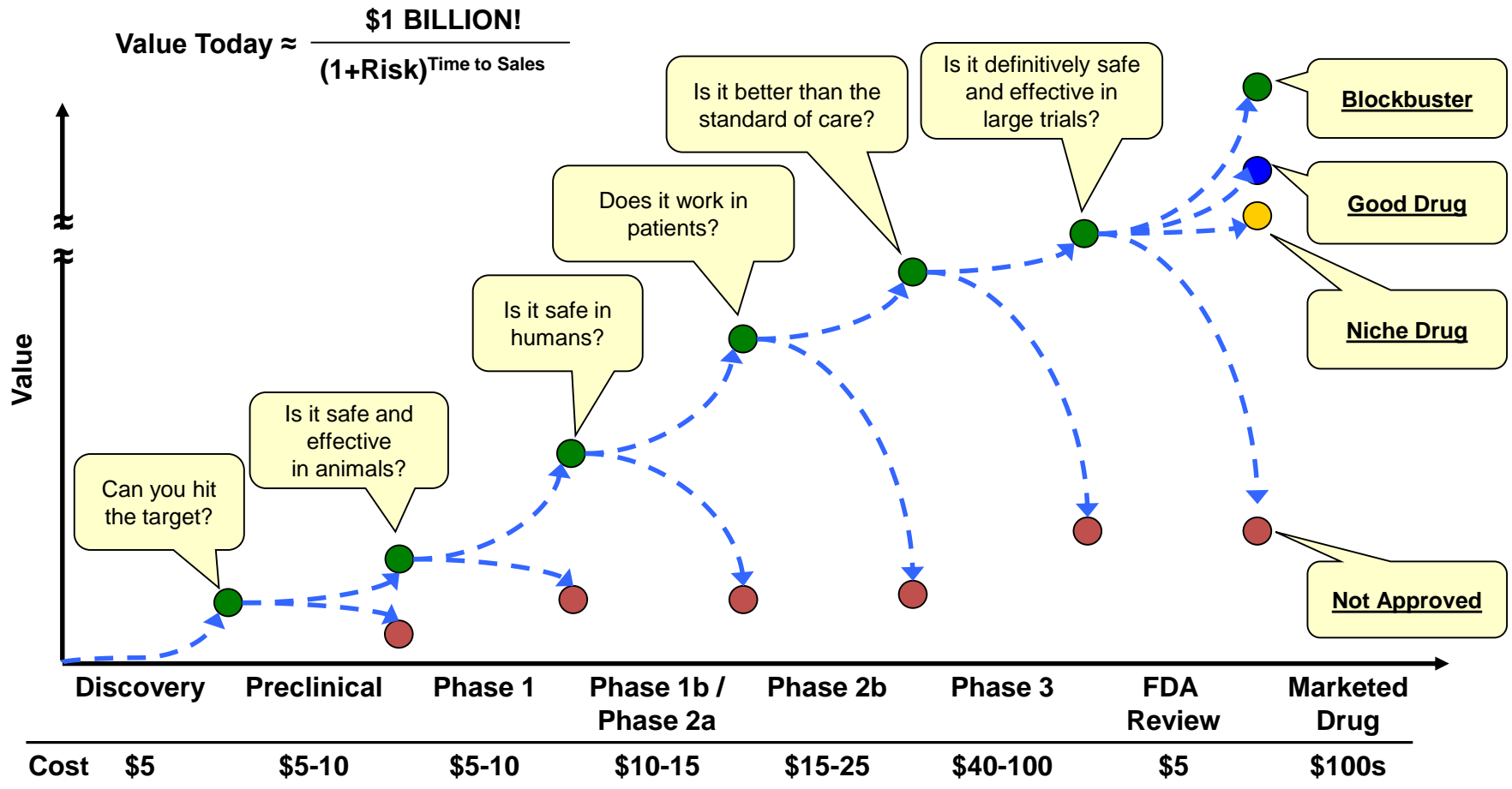
- Sam Hall, Principal at Apple Tree Partners
 - Co-lead Early-Stage Therapeutics practice at Apple Tree; focus is on de-novo company formation
 - Strange mix of prior experience across both basic science and finance
 - Immunologist at University of Cambridge
 - Private equity investor at Symphony Capital
 - Began career as investment banker at Citigroup / Salomon Smith Barney

Topics for Discussion

- How do early-stage biotech companies create value?
- How can we measure it?
- Why do valuation and understanding it matter to the founder / entrepreneur?
- A sketch of how outside equity investment works
- Some thoughts on selection of funding sources
- Discussion / Q&A

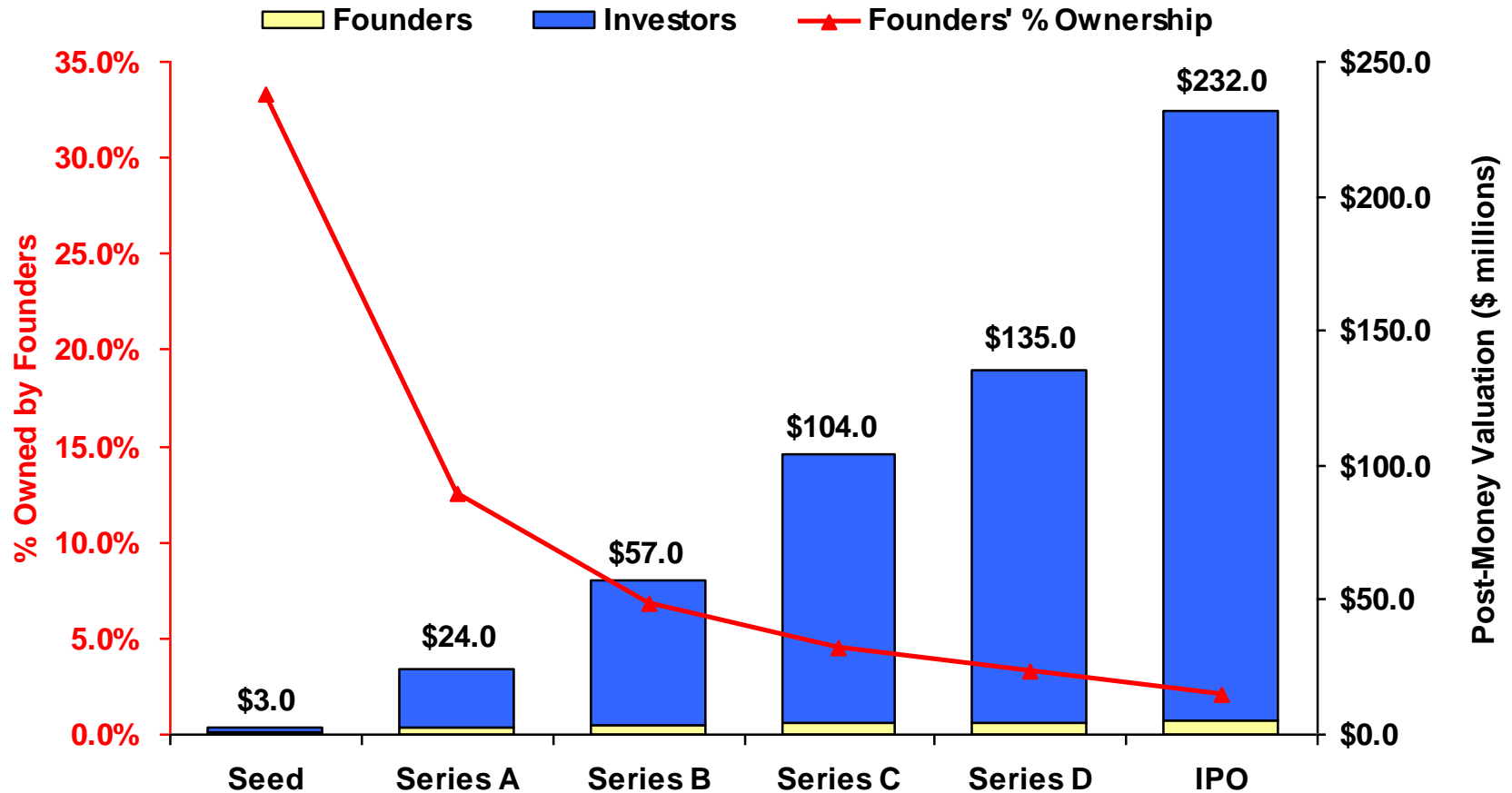
Value and the Biotech Business Model

- Value is driven by asking and answering scientific / clinical questions that reduce the risk you never reach the end of the rainbow....



Why Does Valuation Matter to an Entrepreneur?

- Hypothetical founder's ownership, based on historical median valuations and round sizes



Valuation Involves Very Little Magic...

- Pure and simple arithmetic, with a dash of judgment / artistry
- Three fundamental approaches, with many variations:
 - Discounted Cash Flow Analysis – Intrinsic value of a project / company
 - Comparable Company Analysis – How much similar companies are worth in the efficient public market
 - Precedent Transactions – How much others paid for similar assets
- Valuation can say [almost] whatever you want; it is a tool of argument / negotiation
 - Gaining fluency with valuation will help you achieve objectives in capital raising, partnering transactions and potential M&A

What is a Biotech Project Worth?

Theoretical biotech project: \$1.5 billion in peak sales potential, but very early today

Key Forecast Assumptions

Product Assumptions

Year of Launch	2023
Year of Patent Expiry	2036
Year of Peak Sales	2027
First Year Sales	\$250
Peak Sales	\$1,500
Revenue CAGR to Peak Sales	56.5%

Annual R&D Expense	\$10.0
Base SG&A	\$3.0
COGS / Revenues	10.0%
SG&A / Revenues	25.0%
Tax Rate	37.0%

- Models do not need to be complicated—the simpler, the better
- Very simple assumptions get close to approximating the revenue and profit potential of a project
- Sensitivity analysis can help to identify which assumptions are most important

15-Year Product Forecast

Year Ending December 31,

(\$ in millions)	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Product Revenues	--	--	--	--	--	--	--	\$250.0	\$391.3	\$612.4	\$958.4	\$1,500.0	\$1,500.0	\$1,500.0	\$1,500.0
Cost of Goods Sold	--	--	--	--	--	--	--	25.0	39.1	61.2	95.8	150.0	150.0	150.0	150.0
Gross Profit	--	--	--	--	--	--	--	\$225.0	\$352.1	\$551.1	\$862.6	\$1,350.0	\$1,350.0	\$1,350.0	\$1,350.0
R&D Expense	\$10.0	\$10.0	\$10.0	\$10.0	\$10.0	\$10.0	\$10.0	--	--	--	--	--	--	--	--
SG&A Expense	\$3.0	\$3.0	\$3.0	\$3.0	\$3.0	\$3.0	\$3.0	\$65.5	\$100.8	\$156.1	\$242.6	\$378.0	\$378.0	\$378.0	\$378.0
Operating Income	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	\$159.5	\$251.3	\$395.0	\$620.0	\$972.0	\$972.0	\$972.0	\$972.0
Tax Expense	--	--	--	--	--	--	--	\$59.0	\$93.0	\$146.2	\$229.4	\$359.6	\$359.6	\$359.6	\$359.6
Total Cash Flow	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	\$100.5	\$158.3	\$248.9	\$390.6	\$612.4	\$612.4	\$612.4	\$612.4

Core Concept: Time Value of Money

I lost my wallet and convinced you to lend me \$100.
Which repayment plan sounds better?

Option A:
\$100 This Afternoon

- Money right away
- Little risk

OR

Option B:
\$100 Next November

- I might get hit by a bus
- I might go to Vegas
- I might get sued for my shirt
- Etc.

\$1.00 now is worth \$1.00
\$1.00 later is worth LESS than \$1.00 because there is RISK

For a biotech project, profits usually are in the distant future and getting there is fraught with risk:

\$1,500M in 2030 is NOT worth \$1,500M today

How much less??

Discounted Cash Flow Analysis & Net Present Value

15-Year Product Forecast

(\$ in millions)	Year Ending December 31,														
	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Product Revenues	--	--	--	--	--	--	--	\$250.0	\$391.3	\$612.4	\$958.4	\$1,500.0	\$1,500.0	\$1,500.0	\$1,500.0
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Certain Cash Flow
Uncertain Future Cash Flows

$$\text{Net Present Value} = (\text{Cash Flow})_{2016} + \frac{(\text{Cash Flow})_{2017}}{(1+\text{Risk})^1} + \frac{(\text{Cash Flow})_{2018}}{(1+\text{Risk})^2} + \frac{(\text{Cash Flow})_{2019}}{(1+\text{Risk})^3} + \dots \text{etc} \dots + \frac{(\text{Cash Flow})_n}{(1+\text{Risk})^{(n-2016)}}$$

- Future cash flows need to be “discounted” to reflect their uncertain nature and convert them into 2016 dollars
- But what should be the “discount rate” that reflects this risk?

Accounting for Risk in DCF Analysis

- In finance, discount rates are calculated as the “risk-free rate” (US Treasury), PLUS a premium to reflect the inherent risk in a business that is not the federal government
- Discount Rate = (Federal Funds Rate + Biotech Risk Premium)
- Typical discount rates of 15-20% for development-stage biotech; 8-12% for profitable biotech

15-Year Product Forecast

Year Ending December 31,

(\$ in millions)	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Total Cash Flow	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	(\$13.0)	\$100.5	\$158.3	\$248.9	\$390.6	\$612.4	\$612.4	\$612.4	\$612.4

Certain Cash Flow (2016) | UNcertainty Future Cash Flows (2017-2030)

In Excel: =NPV(Rate,CF₁:CF_n)

Discounted Cash Flow Valuation

Discount Rate

(\$ in millions)	10.0%	12.0%	14.0%	16.0%	18.0%	20.0%	22.0%	24.0%
2016 Product NPV	\$1,060	\$857	\$695	\$565	\$461	\$376	\$307	\$251

Discount rates are a KEY LEVER influencing DCF valuation but nobody can tell you for certain what the discount rate should be...

Comparable Company Valuation

- Can be as simple as “Phase 1 cancer companies have market caps of \$150-\$300M”
- Public market multiples are primarily useful for valuing later-stage companies

Selected Revenue-Stage Biopharma Comparables

Company	Ticker	Current Price	Market Cap	P/E Multiple			TEV/EBITDA Multiple		
				2016E	2017E	2018E	2016E	2017E	2018E
Shire	SHP	\$58.06	\$51,061	13.5x	11.3x	9.6x	15.8x	11.2x	9.9x
Alexion	ALXN	\$135.59	\$30,406	29.1x	23.7x	18.3x	20.7x	18.2x	14.1x
Vertex	VRTX	\$77.58	\$19,242	101.7x	31.9x	17.8x	NM	34.8x	20.1x
Actelion	ATLN	\$144.19	\$14,946	18.5x	18.9x	15.9x	15.6x	16.0x	13.7x
UCB Pharma	UCB	\$67.81	\$12,769	20.7x	16.8x	13.8x	12.9x	11.1x	9.6x
Grifols	GRF	\$18.10	\$12,177	20.8x	18.4x	16.2x	12.9x	11.7x	10.7x
Jazz Pharma	JAZZ	\$113.60	\$6,876	11.3x	10.0x	8.2x	8.3x	7.2x	5.7x
United Therapeutics	UTHR	\$118.14	\$5,011	7.5x	7.3x	8.4x	3.4x	4.2x	6.1x
Acorda	ACOR	\$17.70	\$817	56.6x	31.6x	17.6x	NM	NM	NM
Mean			\$17,034	31.1x	18.9x	14.0x	12.8x	14.3x	11.3x
High			\$51,061	101.7x	31.9x	18.3x	20.7x	34.8x	20.1x
Median			\$12,769	20.7x	18.4x	15.9x	12.9x	11.5x	10.3x
Low			\$817	7.5x	7.3x	8.2x	3.4x	4.2x	5.7x

DISCOUNTED P/E MULTIPLE-BASED VALUATION

Discount Rate **20.0%**

(\$ in millions)	Year	Earnings	P/E Multiple		Future Value		2016 Value	
			Low	High	Low	High	Low	High
2026 Discounted P/E	2026	\$390.6	7.0x	20.0x	\$2,734	\$7,812	\$442	\$1,262
2027 Discounted P/E	2027	\$612.4	7.0x	20.0x	\$4,287	\$12,247	\$692	\$1,978
Mean Value					\$3,510	\$10,029	\$567	\$1,620

Precedent Transactions

- What is a 2-bedroom apartment within 4 blocks of Washington Square worth?
- Valuing a biotech business is no different

The image shows a Zillow real estate map for Manhattan, NY 10002. The map displays various apartment units for sale, with their prices and unit counts labeled. A green shaded area in the center of the map represents Washington Square Park. The map includes street names such as Christopher St, Washington St, and Broadway. The Zillow logo is visible in the top left corner, and the search filters at the top indicate 'Manhattan NY 10002', 'RECENTLY SOLD', '\$1M - \$3M', '2+ BEDS', and 'HOME TYPE (3)'. On the right side of the map, there is a sidebar with the title '10002 Real Estate' and '122 results'. Below the title, there are three property listings, each with a photo, a 'SOLD' price, and details about the unit's features and sale date.

10002 Real Estate
122 results.
Homes for You Newest More

9 photos
SOLD: \$1.74M
Price/sqft: \$1,577 • 2 bds • 1 ba • 1,100 sqft
Sold 10/19/2016 • 114 E 13th St APT 5C, New York, NY

9 photos
SOLD: \$1.59M
Price/sqft: - • 2 bds • 1 ba • - sqft
Sold 10/14/2016 • 35 W 9th St APT 2C, New York, NY

5 photos
SOLD: \$2.23M
Price/sqft: \$1,934 • 2 bds • 2.5 ba • 1,150 sqft
Sold 10/05/2016 • 2 Cornelia St APT 603, New York, NY

A Real-World Example

- What is the appropriate Series A pre-money valuation for Syntimmune?

Seed / Series A Comparable Company Financings

Company Name	Financing Date	Financing Type	Company Focus	Amount Raised	Pre-Money Valuation	Post-Money Valuation
Atrean	2013	Series A	Biologics for autoimmune diseases	\$20.0	\$8.0	\$28.0
Peloton Therapeutics	2011	Series A	Early stage cancer therapy	18.0	8.0	26.0
Kala Pharmaceuticals	2012	Seed	Novel ophthalmic formulation / delivery	11.3	7.7	19.0
Permeon Biologics	2011	Series A	Intracellular delivery of biologics	5.1	7.6	12.7
ALDEA Pharmaceuticals	2013	Series A	Drugs modulating aldehyde metabolism	11.4	7.6	19.0
Seres Health	2012	Series A	Antibody-based therapies for cancer	6.5	7.0	13.5
Thesan Pharmaceuticals	2012	Series A	Dermatological drug developer	16.0	6.3	22.3
Palkion	2008	Series A	Therapies for treatment of anemia	8.7	6.3	15.0
Ra Pharmaceuticals	2012	Series A	Peptides targeting protein-protein interactions	18.9	6.1	25.0
Confluence Life Sciences	2012	Series A	Kinase inhibitors for cancer and inflammation	4.2	5.5	9.7
Madison Vaccines	2014	Series A	DNA vaccines for prostate cancer	8.0	5.5	13.5
OncoPep	2012	Series A	Cancer vaccines	5.0	5.5	10.5
Vanquish Oncology	2014	Series A	Targeted cancer therapies	4.4	5.3	9.6
Kurobe Pharmaceuticals	2013	Series A	Novel antibiotics for resistant infections	5.0	5.2	10.2
Lysosomal Therapeutics	2014	Seed	Small molecules for neurodegeneration	4.8	5.1	9.9
Protagonist Therapeutics	2013	Series A	Developer of peptide and peptidomimetic therapies	9.0	4.7	13.7
Igenica	2009	Series A	Novel antibody discovery platform	6.2	3.3	9.5
High				\$20.0	\$8.0	\$28.0
Mean				9.6	6.2	15.7
Median				8.0	6.1	13.5
Low				4.2	3.3	9.5

More Real-World...

- What valuation step-up is fair for Syntimmune's Series B financing?

SELECTED PRECEDENT SERIES B VALUATIONS & STEP-UPS

Company Name	Date	Series	Pre-Money Valuation	Deal Size	Post-Money Valuation	Prior Post-Money	Value Step-Up
Artax Biopharma	09/22/15	Series B	\$24.3	\$10.0	\$34.3	\$12.0	2.0x
REGENXBIO (RGNX)	11/07/13	Series B	21.3	7.9	29.2	10.9	2.0x
Seres Therapeutics	06/06/14	Series B	53.9	10.6	64.5	27.6	2.0x
OncoPep	08/28/14	Series B	17.9	6.9	24.8	11.9	1.5x
Santa Maria Biotherapeutics	01/13/14	Series B	35.3	24.3	59.6	24.3	1.5x
ImmusanT	12/30/14	Series B	40.0	12.7	52.7	32.7	1.2x
Ignyta (RXDX)	02/01/13	Series B	7.5	5.5	13.0	6.3	1.2x
Velicept Therapeutics	12/01/15	Series B	25.1	21.0	46.1	21.0	1.2x
Aclaris Therapeutics	10/02/14	Series B	50.0	21.0	71.0	41.9	1.2x
Complexa	06/04/14	Series B	21.2	14.8	36.0	18.5	1.1x
Peloton Therapeutics	12/18/13	Series B	35.0	12.6	47.6	30.6	1.1x
Cerecor	07/18/14	Series B	50.1	16.3	66.3	45.2	1.1x
Pinta Biotherapeutics	01/13/14	Series B	39.1	24.3	63.4	35.6	1.1x
Blend Therapeutics	12/23/13	Series B	21.5	21.0	42.5	23.8	0.9x
Allena Pharmaceuticals	11/12/14	Series B	35.3	25.0	60.3	40.3	0.9x
Iconic Therapeutics	04/16/14	Series B	20.0	20.2	40.2	31.4	0.6x
Edimer Pharmaceuticals	07/30/13	Series B	21.7	18.0	39.7	40.0	0.5x
Protagonist Therapeutics	09/19/13	Series B	11.0	18.0	29.0	27.0	0.4x
High			\$53.9	\$25.0	\$71.0	\$45.2	2.0x
Mean			29.5	16.1	45.6	26.7	1.2
Median			24.7	17.1	44.3	27.3	1.2
Low			7.5	5.5	13.0	6.3	0.4

Even More Real-World...

- When and at what valuation would we consider selling Syntimmune?

Selected Early-Stage M&A Transactions

Target	Acquirer	Therapeutic Area	Year	Phase at Acquisition	Up-Front	Total Consideration
Flexus Biosciences	Bristol-Myers Squibb	Oncology	2015	Preclinical	\$800.0	\$1,250.0
Padlock	Bristol-Myers Squibb	Inflammation	2016	Preclinical	\$225.0	\$600.0
Amplimmune	AstraZeneca	Oncology	2013	Preclinical	\$225.0	\$500.0
Heptares	Sosei	CNS	2015	Phase 1	\$180.0	\$400.0
Lotus Tissue Repair	Shire	Orphan	2013	Preclinical	\$49.0	\$325.0
Costim	Novartis	Oncology	2014	Preclinical	\$95.0	\$248.0

Selected Precedent M&A Transactions

Target	Acquirer	Indication	Year	Phase at Acquisition	Valuation	Comments
ViroPharma	Shire	HAE	2013	Marketed	\$4,200.0	Cinryze, the primary driver of the acquisition, was marketed and generating sales of >\$400 million per year. Shire acquired to consolidate HAE market.
Lev Pharmaceuticals	ViroPharma	HAE	2008	Approved	\$617.5	Company was formed exclusively to develop the C1 esterase inhibitor, Cinryze for HAE. Targeted, virtual development led by Judson Cooper et al. Acquired for asset shortly after approval
Jerini	Shire	HAE	2008	NDA	\$521.0	Sole asset was Friazyr, a peptidomimetic bradykinin antagonist for HAE, which was pending EU approval at the time of acquisition.
Lotus Tissue Repair	Shire	Epidermolysis Bullosa	2013	Preclinical	\$324.4	Virtual startup around enzyme replacement for epidermolysis bullosa, a rare blistering disease. Project grew in part out of their earlier attempt to license Dyax anti-FcRn antibody. Valuation includes \$275M clinical milestones.

Valuation Isn't Everything

- Be equipped to convincingly address valuation with potential investors, partners, acquirors, etc., but do not be myopic



- ATP spin-out from Krainer lab at Cold Spring Harbor
 - Novel application of proven antisense chemistries
 - No data at inception
 - No plan
- Do you choose higher valuation or technical & company-building expertise?

An Evolving Company Needs More Than Cash

	Conception / Gestation	Infancy	Adolescence	Maturity
Assets	<ul style="list-style-type: none">• Idea / initial IP• Technical / management expertise	<ul style="list-style-type: none">• Company founded• Idea advancing• Clear development / implementation plan• Seed capital in place	<ul style="list-style-type: none">• Growing company, capable team• Idea / intellectual property progressing• Clinical data• Supportive VC investor base	<ul style="list-style-type: none">• POC data• Growing pipeline• Lead candidates in Phase 2 / 3• Corporate organization with strong management
Needs	<ul style="list-style-type: none">• Capital• Structure• Management	<ul style="list-style-type: none">• Capital to fund advancing programs• Governance• Entrepreneurial expertise• Contacts• Structure	<ul style="list-style-type: none">• Capital to fund later stage / larger trials• Proof of concept data• Additional expertise	<ul style="list-style-type: none">• Even more capital• Commercial capabilities• Liquidity for founders and VC investors

APPENDIX



Mechanics of Seed and Series A Funding

