# Proposed investment strategy: development milestones

Raymond Chiasson

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- Small portfolio performance

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# Proposal: purchase development stage milestones from biotechs

Biotechs or biotech investors often find themselves entitled to contingent payments upon the sale of assets or the company (royalties and milestones)

Milestones are payments made upon the achievement of certain developmental, regulatory or commercial events

Holders of these contingent payments have an interest in monetizing at least a portion of these payments to fund other operations, mitigate risk, crystalize returns, etc.

### Sample recent deal with milestones

UroGen Pharma Announces Exclusive License Agreement with Agenus Inc to Advance Treatment of Urinary Tract Cancers

November 11, 2019, 8:00 a.m. EST	
SHARE THIS ARTICLE	UroGen Pharma Announces Exclusive License Agre Advance Treatment of Urinary Tract Cancers
Share	UroGen to Develop and Commercialize Zalifreli
<b>y</b> Tweet	antibody)with UGN-201 for High-Grade Non-Musc

	Product	zalifrelimab
ei	Upfront	\$10M
ii c	Development milestones	\$115M
	Commercial milestones	\$85M
	Royalties	14-20%

# Royalties & commercial milestones are tough to value/monetize at early stages

- The product must advance all the way to commercialization
- Sales forecasting must be done without knowing the product's clinical profile, the future competitive environment, treatment approach, etc.

# Monetizing development milestones is fundamentally different

- Product may only need to meet 1 or 2 milestones to make a solid return
- Outcomes are nearer-term
- Development risk is isolated from commercial risk; no commercial forecasting is required

# Why this is an attractive opportunity

#### Attractive returns and deal characteristics

- For individual deals: 5-15% chance of >8x multiple; 15-45% chance of multiple of at least ~2x
- For small portfolio: median returns of 1.6-2.1x and 30-49% IRR with most return paid out by year 6
- Guaranteed cash exit with predictable timing
- Numerous readouts (milestones) in each deal reduces variance
- Level of risk can be tuned by focusing on deals at certain maturities (e.g. focusing on phase 2 assets instead of pre-clinical)

#### Fits with VC investor's experience & core competencies

- Exposure is to development risk on early/mid-stage products
- Forecasting requires predicting binary events tied to clinical development
- Leverage network of connections to source deals

#### Easy add-on to current strategy

- Requires no active portfolio company management
- Risk profile is similar enough to sit with traditional VC investments as strategy is built
- Large deal universe: ~25-30 transactions per year with circumstances suitable to this strategy<sup>1</sup>, and the value of development milestones per deal has nearly doubled since last decade<sup>2</sup>

# Deal universe

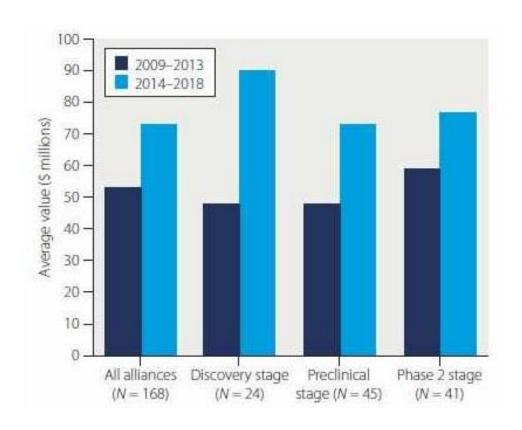
# ~25-30 deals per year with circumstances suitable to this strategy<sup>1,2</sup>

- Asset transaction with milestone component
- Product at suitable stage of development

# Average deal and milestone sizes for two deal types as defined by BioPharma Dealmakers (2014-2018)

Component	Discovery (mean)	Preclinical (mean)
Deal size	703	144
Upfront	64	6
Total development milestones	90	73
Phase 3 start	20	13
First approval	48	19

The size of development milestones has increased considerably for the period 2014-2018 compared to the previous 5-year period<sup>2</sup>



<sup>1.</sup> GlobalData deals database 2009 - 2019

<sup>2.</sup> BioPharma Dealmakers deals with milestones

# Typical milestones & single deal outcomes

### **Simplified set of potential milestones**

Component	Value (\$M) <sup>2,3</sup>	Timing (years from deal) <sup>4</sup>	Probability of advancing <sup>5,6</sup>
Phase 1 initiation	3.5	1	32.0%
Phase 2 initiation	7	3	63.2%
Phase 3 initiation	14	5	30.7%
First approval	19	8	49.6%

#### Notes:

- 1. Potential outcomes based on deals including 2, 3 or 4 milestones from the simplified set.
- 2. Phase I and phase 2 milestones assumed based on review of a sample of license agreements.
- 3. Phase 3 and first approval milestones taken from Biopharma dealmakers analysis for year 2014-2018.
- 4. Timing is estimated based on typical development timelines from discovery stage to first regulatory approval.
- 5. Probabilities for phase 2 to approval are based on June 2016 BIO report; higher success rates have been reported more recently by Lo et al. 2018.
- 6. Probabilities for phase I initiation are hard to estimate given lack of public data and an unclear starting point. Takebe et al. 2018 estimates a 32% probability for preclinical work. Assume that milestones would not be bought until advancing to that preclinical stage.

# Potential single deal outcomes<sup>1</sup>

Outcome	Performance	Probability
Home run	>8x multiple >120% IRR	5-15%
Middle groud	1.6-7.4x multiple >50% IRR	15-45%
Total loss	0x multiple	35-70%

# Potential outcomes at portfolio level

# Sample portfolio of 5 potential deals with typical outcomes

		Deal 1	Deal 2	Deal 3	Deal 4	Deal 5
	Approval	26	35	36	22	33
Events &	Phase 3 init	19	26	26	16	24
value	Phase 2 init		13 🗸	13 🗸	8	12 🗸
	Phase 1 init				4	6 🗸
	Upfront	4.8	8.1	8.1	1.6	2.4
Doutoumoneo	Payouts	0	13	13	0	18
Performance	Multiple	0	1.6	1.6	0	7.4
	IRR	-	61%	60%	-	202%

# **Portfolio performance**

Portfolio		
Approval	152	
Phase 3 init	111	
Phase 2 init	46	
Phase 1 init	10	
Upfront	25	
Payouts	44	
Multiple	1.8	
IRR	49%	

#### Notes:

- 1. Portfolio performance is based on the success of milestones with a checkmark.
- 2. Deal outcomes were picked from a semi-random sample of near-median return scenarios.
- 3. Full deal and portfolio assumptions described in appendix.

# Portfolio performance distribution

### Range of portfolio performance<sup>1</sup>

Likely downside			
Percentiles	25-30 <sup>th</sup>		
Payouts	25 – 26		
Multiple	1.0x		
IRR	0 – 4%		

Median		
Percentiles	45-55 <sup>th</sup>	
Payouts	41 – 52	
Multiple	1.6 – 2.1x	
IRR	30 – 49%	

Likely upside		
Percentiles	70-75 <sup>th</sup>	
Payouts	72 – 81	
Multiple	2.9 – 3.2x	
IRR	66 – 74%	

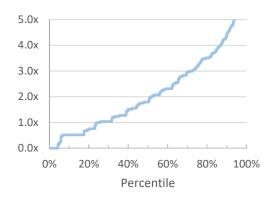
Worst case		
Percentiles	<10 <sup>th</sup>	
Payouts	0 – 13	
Multiple	0 - 0.5x	
IRR	-	

Best Case		
Percentiles	>90 <sup>th</sup>	
Payouts	107 - 257	
Multiple	4.3 – 10.3x	
IRR	102 - 167%	

#### **Notes:**

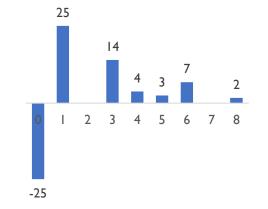
- 1. Payouts, multiples and IRR are calculated for 10k simulations of 5-deal portfolios. Full deal and portfolio assumptions described in appendix.
- 2. Cash flows calculated using average cash flows across all simulations. Does not reflect any individual possible outcomes. No milestones paid in year 2 due to timing and deal assumptions; payments likely spread out in years 1 and 2 in real scenarios.

### **Ordered portfolio multiples**



 Sorted portfolio multiples from 10k simulations of 5deal portfolios

# Average cash flows by year<sup>2</sup>



- Principal recovered in years 1-2
- Return generated in years 3-5
- 'Lottery ticket' milestones read out in years 6-8 (if ever)

# Conclusions/next steps

#### **Preliminary modelling supports attractive financials**

- Individual deal returns are comparable to typical VC investments (5-15% chance of home run, significant chance of total failure)
- Building a small portfolio reduces the impact and likelihood of downside scenarios and centers around favorable median returns

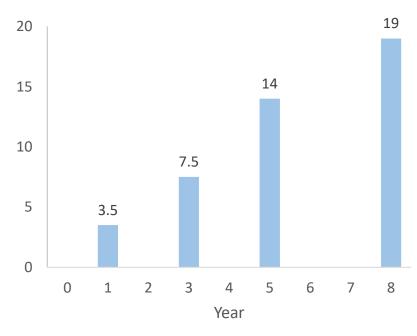
#### **Next step: validate opportunity set**

- Analyze universe of potential sellers (look at relevant deals from last ~5 years)
- Contact potential sellers and explore interest in monetization

# Appendix

# Calculating deal upfronts

# **Potential payouts**

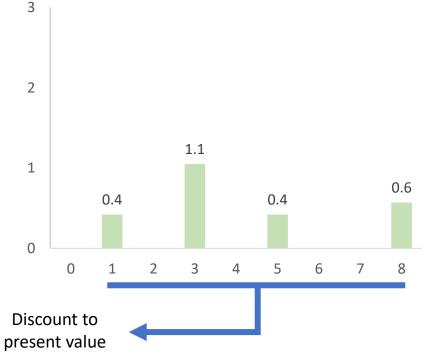


# 3

Multiply by

probabilities

**Expected values** 



# Individual deal characteristics & outcomes

#### **Deal with 4 milestones**

Highest Milestone Achieved	Probability <sup>1</sup>	Total Payout (\$M)	Multiple	IRR	Upfront (\$M)²
approval	3%	43.5	30.8	210%	0.2
phase 3	3%	24.5	17.3	210%	0.2
phase 2	14%	10.5	7.4	202%	0.7
phase 1	12%	3.5	2.5	148%	0.4
none	68%	0	0		
Expected values		4.0 <sup>3</sup>	2.8 <sup>3</sup>	15% <sup>4</sup>	1.4 <sup>5</sup>

#### **Notes:**

- 1. Listed probabilities are the odds of achieving exactly that milestone and are calculated using BIO 2016 and Takebe et al 2018.
- 2. Portion of the total upfront corresponding to each milestone.
- 3. Payout and multiple weighted average are calculated according to the listed probabilities
- 4. Weighted average IRR corresponds to whatever discount rate is used. In any individual deal, it will be 0% or very large.
- 5. Total deal cost that one would pay for the series of milestones
- 6. Payout of the first milestone is assumed to occur I year after the deal

#### **Deal with 3 milestones**

Highest Milestone Achieved	Probability <sup>1</sup>	Total Payout (\$M)	Multiple	IRR	Upfront (\$M)²
approval	10%	40	8.9	130%	0.9
phase 3	10%	21	4.7	121%	0.9
phase 2	44%	7	1.6	56%	2.7
none	37%	0	0		
Expected values		9.03	2.03	15% <sup>4</sup>	4.5 <sup>5</sup>

#### **Deal with 2 milestones**

Highest Milestone Achieved	Probability <sup>1</sup>	Total Payout (\$M)	Multiple	IRR	Upfront (\$M)²
approval	15%	33.0	8.7	301%	1.9
phase 3	15%	14.0	3.7	270%	1.9
none	69%	0	0		0.0
Expected values		7.2 <sup>3</sup>	1.9 <sup>3</sup>	15% <sup>4</sup>	3.8 <sup>5</sup>

# Portfolio simulation assumptions

Parameter	Possible values	Rationale
Number of deals	5	Assume 5 deals are completed on 5 sets of milestones
Milestone values	Phase 1 init 3.5 - 7  Phase 2 init 7 - 14  Phase 3 init 14 - 28  Approval 19 - 38	<ul> <li>Expect some variability in deal size for real portfolios; assuming equal deal size reduces/underestimates variance</li> <li>Assume deals are randomly distributed across these ranges</li> <li>Ratio of milestone sizes is maintained</li> <li>The lower end of the range corresponds to average values from biopharma dealmakers data for 2014-2018. Using a set of up to 2x as large to create reasonable range of deal sizes (2-10M upfront each)</li> </ul>
Number of milestones	2, 3, 4	<ul> <li>Corresponding to doing deals at preclinical, phase 1 or phase 2 stage</li> <li>Select deals randomly</li> </ul>
Possible timings	at pre-clinical stage after phase 1 initiation after phase 2 initiation	<ul> <li>2 years between phase 1 and phase 2</li> <li>2 years between phase 2 and phase 3</li> <li>3 years between phase 3 and approval</li> <li>Assume deal is always done 1 year from the next possible milestone</li> </ul>
Probability of success at each stage	Phase 1 init 32% Phase 2 init 63% Phase 3 init 31% Approval 50%	<ul> <li>Same values from BIO 2016 and Takebe et al 2018</li> <li>Outcomes are simulated based on these probabilities</li> </ul>
Discount rate	15%	Assumption for target expected return

# Expected deal metrics at each stage

Stage of deal	Milestones remaining	Upfront (\$M)	Multiple	Payout (\$M)	Total possible payout (\$M)	% of sticker price (upfront/total possible)	Probability of hitting at least one milestone	Min IRR if successful
Preclinical	4	1.4	2.8x	4.0	43.5	3.2%	32%	148%
Phase 1	3	4.5	2.0x	9.0	40.0	11.3%	63%	56%
Phase 2	2	3.8	1.9x	7.2	33.0	11.5%	31%	270%

# Portfolio performance distribution: 5-deal portfolios versus 10-deal portfolios

Worst o	Worst case: Percentiles <10 <sup>th</sup>				
	5-deal 10-deal				
Payouts	0-13	0 – 22			
Multiple	<b>Multiple</b> 0 - 0.5x 0 - 0.85x				
IRR	-	-			

Likely dow	Likely downside: Percentiles 25-30 <sup>th</sup>				
	5-deal 10-deal				
Payouts	25 – 26	33 – 38			
Multiple	1.0x	1.3x – 1.5x			
IRR	0 – 4%	16 – 23%			

Median: Percentiles 45-55 <sup>th</sup>						
	5-deal 10-deal					
Payouts	41 – 52	48 – 56				
Multiple	ti <b>ple</b> 1.6 – 2.1x 1.9 – 2.2x					
IRR	30 – 49%	36 – 45%				

Likely up	Likely upside: Percentiles 70-75 <sup>th</sup>				
	5-deal 10-deal				
Payouts	72 – 81	67 – 73			
Multiple	2.9 – 3.2x	2.7 – 2.9x			
IRR	66 – 74%	58 – 63%			

Best case: Percentiles >90 <sup>th</sup>					
	5-deal 10-deal				
Payouts	107 - 257	92 – 181			
Multiple	4.3 – 10.3x	3.7 – 7.2x			
IRR	102 - 167%	82 - 147%			

# A larger portfolio decreases likelihood of downside scenarios

	Single deal (4 milestones)	5 deal portfolio (16 milestones)	10 deal portfolio (32 milestones)
Total loss	68%	4%	<0.1%
50% loss	68%	7%	2%
Not breakeven	32%	26%	15%
% above 2x multiple	20%	48%	53%