New Perspectives in Pediatric Oncology Drug Development

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Pipeline & Portfolio Planning
Children with Cancer do not have Timely Access to Safe and Efficacious Drugs

Our Vision

- Provide children with unmet medical needs with innovative, safe, life-saving therapies

Our Missions

- Ensure **early access** to drugs for children with high unmet medical needs
- Improve pediatric patient care through **pediatric product labeling**
- Fulfill pediatric regulatory obligations to ensure **timely registrations in adults**
- Ensure **financial sustainability** through incentives and rewards
Provide Children with Unmet Medical Needs with Innovative, Safe, Life-savings Therapies

A stepwise approach to fulfill our vision

**High Hanging Fruit**
develop pediatric-specific drugs

**Medium Hanging Fruit**
repurpose “shelved” drugs

**Low Hanging Fruit**
ensure all drugs with a pediatric rationale are available to children

**Key activities**

- Business valuation on repurposed drug
- Innovative funding mechanisms

**Key activities**

- Pediatric Preclinical Screening Platform
- Innovative clinical trial implementation
- Improve access to Adolescents and Young Adults

Collaboration with Academia
In/Out-licensing
Where to?

Mechanism of Action-based pediatric drug development

Pediatric assets prioritization across industry’s portfolio

Early entry in children through adapted incentives

Innovative business models for “pediatric-only” approaches
There are actually several elephants in the room…

*but a critical one is funding pediatric R&D in a sustainable way*
Pediatric Business Valuation Pilot

*This pilot aims to better understand the value of pediatric development opportunities and key value drivers*

Key Objectives

1. **Valuation Basics**: introduction to aNPV and RR
2. **Valuation Drivers**: identify key value drivers of pediatric programs
3. **Valuation Trade-offs**: use scenarios to understand the impact of different drivers
4. **How to use valuation**: apply valuation insights to select drug candidates
Valuation Basics

Introduction to aNPV

Valuation is Adjusted Net Present Value (aNPV)

- **Unmeet Need**: Size of patient population in unmet need
- **Dev. Costs**: Financial investment needed
- **Dev. Time**: Timing to develop and make available for patients
- **Risk**: Clinical and regulatory uncertainties

What does the valuation do?

Quantifies the extent to which a drug candidate and its development can successfully deliver a treatment that is approved by regulators, brings meaningful benefit to patients, is prescribed by physicians and offsets risks and costs.

Why is aNPV useful?

aNPV can help us make thoughtful decisions on promising development opportunities that in addition to addressing an unmet need today, ensure financial sustainability for future opportunities in other areas of high unmet need.
Valuation Basics

*We use aNPV as a tool to measure the multiple components of a program’s value.*

**ILLUSTRATIVE**

Two critical factors:
- Time to Launch
- Probability of Launch

6month LOE Extension

Amount

Cost
Sales

Launch

Non-discounted cash flow

Discounted for time value of $ & program risk

Discounted for time value of $
Valuation Basics

Introduction to RR

**RR is Return Ratio**

What does the RR do?

Measures whether the investment costs can be recuperated and informs us where we can expect to get the most return per unit invested.

What does RR Mean?

<table>
<thead>
<tr>
<th>RR</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0</td>
<td>Loss</td>
</tr>
<tr>
<td>0</td>
<td>Break-even</td>
</tr>
<tr>
<td>1</td>
<td>1 for 1</td>
</tr>
</tbody>
</table>
Valuation Basics
From adult to pediatric centric valuations

Adult-Centered Valuation

Adult development

Pediatric development

Pediatric valuation is dependent on the adult valuation

Pediatric development

Pediatric-centered Valuation

Adult development

Pediatric development

Pediatric valuation is independent on the adult valuation
Valuation Drivers

Understanding key value drivers of pediatric programs

Pediatric Key Valuation Drivers

- Unmet Need
- Dev. Costs
- Risk
- Dev. Time

Other Potential Drivers

<table>
<thead>
<tr>
<th>Priority Review Voucher</th>
<th>Bundled Filings</th>
<th>Academic collaborations</th>
</tr>
</thead>
</table>
Valuation Drivers: Unmet Need
Understanding key value drivers of pediatric programs

## Assumptions on the Size of the Unmet Need (US data)

<table>
<thead>
<tr>
<th>High: 3,200 pts/yr</th>
<th>Med: 800 pts/yr</th>
<th>Low: 320 pts/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Large indication</td>
<td>▪ Mid-size indication</td>
<td>▪ Small indication</td>
</tr>
<tr>
<td>▪ Roughly ~20% of total pediatric cancer patients</td>
<td>▪ Roughly ~5% of total pediatric cancer patients</td>
<td>▪ Roughly &lt;2% of total pediatric cancer patients</td>
</tr>
<tr>
<td>▪ Example: ALL</td>
<td>▪ Example: Neuroblastoma</td>
<td>▪ Example: Desmoplastic small round cell tumor</td>
</tr>
</tbody>
</table>

Assumed total pediatric patients diagnosed per year, age 0-19: 16,000

## Other Assumptions on Patients/Treatment

- Dosing and Duration
- Competition and share of patients
- Persistence and Compliance
- Priority Review Vouchers
Valuation Drivers: Development Costs

*Understanding key value drivers of pediatric programs*

### Assumptions on Range of Development Costs

<table>
<thead>
<tr>
<th>High: 75 mUSD</th>
<th>Med: 50 mUSD</th>
<th>Low: &lt; 30 mUSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Large, randomized study</td>
<td>▪ IST</td>
<td>▪ Academic collaborations</td>
</tr>
</tbody>
</table>

### Assumptions on Other Development Costs

- Full-time Employees
- Filing Costs
- Marketing and Distribution Costs
- General and Administrative costs
- Technical and Manufacturing
- Taxes
- Others
# Valuation Drivers: Risk

*Understanding key value drivers of pediatric programs*

## Assumptions on Clinical and Regulatory Risk

<table>
<thead>
<tr>
<th>High Risk: 5% POL</th>
<th>Med Risk: 10% POL</th>
<th>Low Risk: 30% POL</th>
</tr>
</thead>
</table>

### POL: Probability of Launch

- No data available
- Formulation challenges
- Unknown mechanism of action
- Changes in design from one Ph to the next
- Safety risks
- Negative data in adults
- Negative data for similar agents

- Strong pre-clinical data
- Success in other studies
- Adult data available
- Success in agents in same class
- Promising results from previous phase
- Diagnostic data
- Clear regulatory pathway

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* Probability of Success by Phase and for Launch: KMR Success from General Metrics Study, Industry Rates
Valuation Drivers: Time
Understanding key value drivers of pediatric programs

Assumptions on Development Time

<table>
<thead>
<tr>
<th>Ph1/2</th>
<th>Ph2/Pivotal</th>
<th>Filing/Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPI-LPI: 2 yrs</td>
<td>FPI-LPI: 3 yrs</td>
<td>FDA Review: 8-12 months</td>
</tr>
<tr>
<td>Data base lock and file data: 24 weeks</td>
<td>Data base lock and file data: 24 weeks</td>
<td>Success in other studies</td>
</tr>
<tr>
<td>Follow-up (min): 2 yrs</td>
<td>Follow-up (min): 2 yrs</td>
<td>EMA Review: 12-15 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No wait for follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

~ 7-10 years
**aNPV Matrix**

*Illustrates specific conditions where pediatric development is sustainable*

<table>
<thead>
<tr>
<th>Size of Unmet Need ( #of patients)</th>
<th>Small (320 pts/yr)</th>
<th>Mid (800 pts/yr)</th>
<th>Large (3,200 pts/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dev Costs mUSD</td>
<td>- 15</td>
<td>- 10</td>
<td>5</td>
</tr>
<tr>
<td>30</td>
<td>- 10</td>
<td>- 10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>- 5</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>- 20</td>
<td>- 15</td>
<td>- 5</td>
</tr>
<tr>
<td>50</td>
<td>- 15</td>
<td>- 10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>- 10</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>- 25</td>
<td>- 20</td>
<td>- 10</td>
</tr>
<tr>
<td>75</td>
<td>- 20</td>
<td>- 15</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>- 15</td>
<td>- 5</td>
<td>50</td>
</tr>
<tr>
<td>POL %</td>
<td>5%</td>
<td>10%</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>10%</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>1%</td>
<td>30%</td>
</tr>
</tbody>
</table>

- Based on assumptions, sustainable pediatric development is possible for mid and large indications with high POLs
- Size of patient population and POL are key value drivers

*Numbers rounded off for simplicity*
**RR Matrix**

*Illustrates specific conditions where pediatric development is sustainable*

<table>
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</thead>
<tbody>
<tr>
<td>Dev Costs mUSD</td>
<td>-1</td>
<td>-1</td>
<td>1</td>
</tr>
<tr>
<td>30</td>
<td>-1</td>
<td>-1</td>
<td>1</td>
</tr>
<tr>
<td>50</td>
<td>-1</td>
<td>-1</td>
<td>1</td>
</tr>
<tr>
<td>75</td>
<td>-1</td>
<td>-1</td>
<td>1</td>
</tr>
</tbody>
</table>

| POL % | 5% | 10% | 30% | 5% | 10% | 30% | 5% | 10% | 30% |

- Based on assumptions, sustainable pediatric development is possible for mid and large indications with high POLs
- Size of patient population and POL are key value drivers

* Numbers rounded off for simplicity
Valuation Trade-offs

Valuation model can be used to understand impact of different drivers on a particular scenario

For a drug candidate with a high POL, we can invest more funds and still make it sustainable, compared to a drug candidate with low POL where we need to keep costs extremely low.
How to use this valuation

Valuation model can provide rough guidance on key questions of drug development

For a drug candidate targeting a larger patient population, we can keep cost to patient much lower compared to the cost to patient needed to remain sustainable in small patient population.

* Assumes 10% POL (med) and 50mUSD in development costs (med).
Size of Patient Population and POL are Key Value Drivers

Key Drivers of POL

- Strong pre-clinical data
- Success in other studies
- Adult data available
- Success in agents in same class
- Promising results from previous phase
- Diagnostic data
- Clear regulatory pathway

While the time and costs of development are important considerations, their impact to the valuation is smaller compared to the impact of size of the patient population and the POL.
Doing Now What Patients Need Next

Children