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MEDICINES 4 KIDS PHARMA

2025 Patent Colloquium

Patents & Open Science in New Drug Innovation

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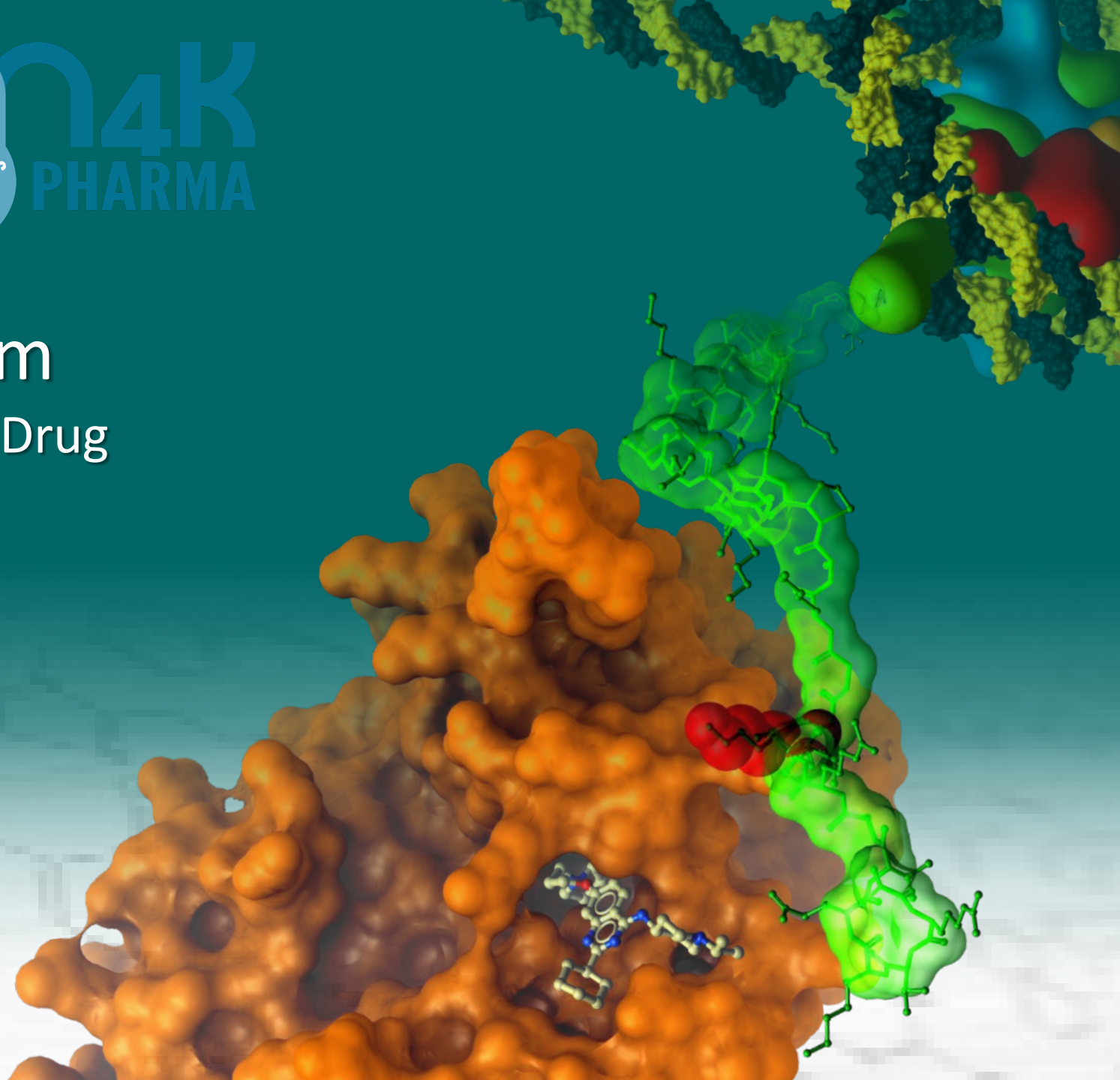


PERSPECTIVE on PATENTS in DRUG DEVELOPMENT

The patent system is an economic policy tool to incentivize the creation of more information goods, with the aim of improving social welfare in the long run.

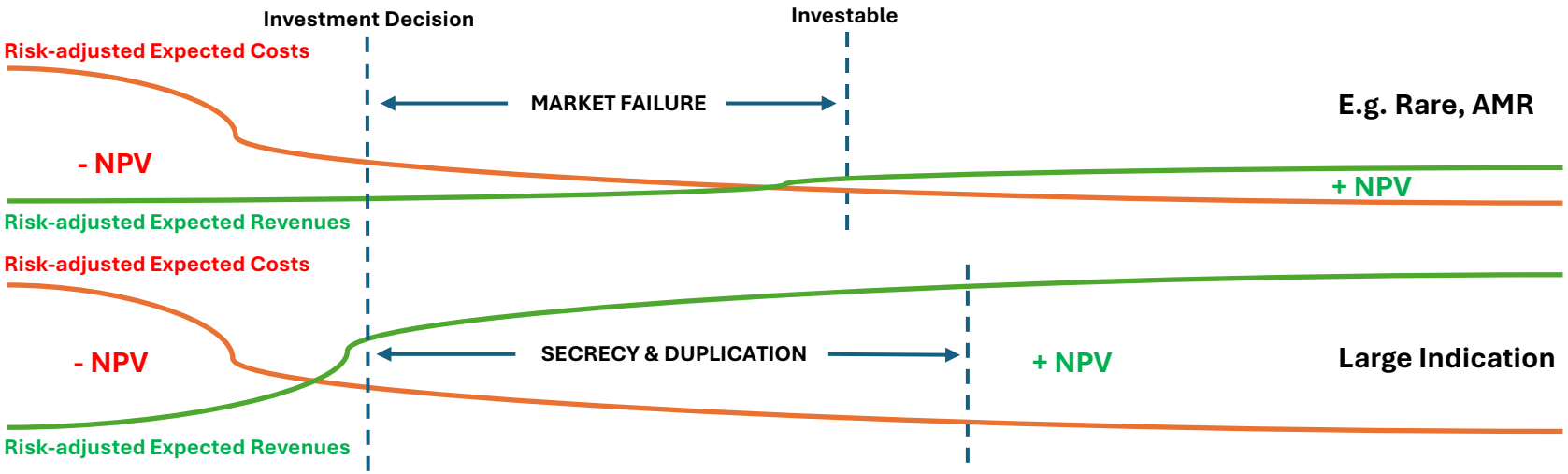
It does so, in theory, by making new information goods excludable for a period of time, thereby preventing free-riding on the investment required to generate the information goods in the first place.

Like any policy tool, we should ask if we're getting the results we want:

In the pharmaceutical industry, is the patent system efficiently and cost effectively delivering new drugs for society's most significant unmet therapeutic needs?

The answer is a mixed bag: patents play a significant incentive role in many areas, while failing in others and giving rise to a number of undesirable pathologies.

A Closer Look at Information Goods in the Pharma Innovation Lifecycle

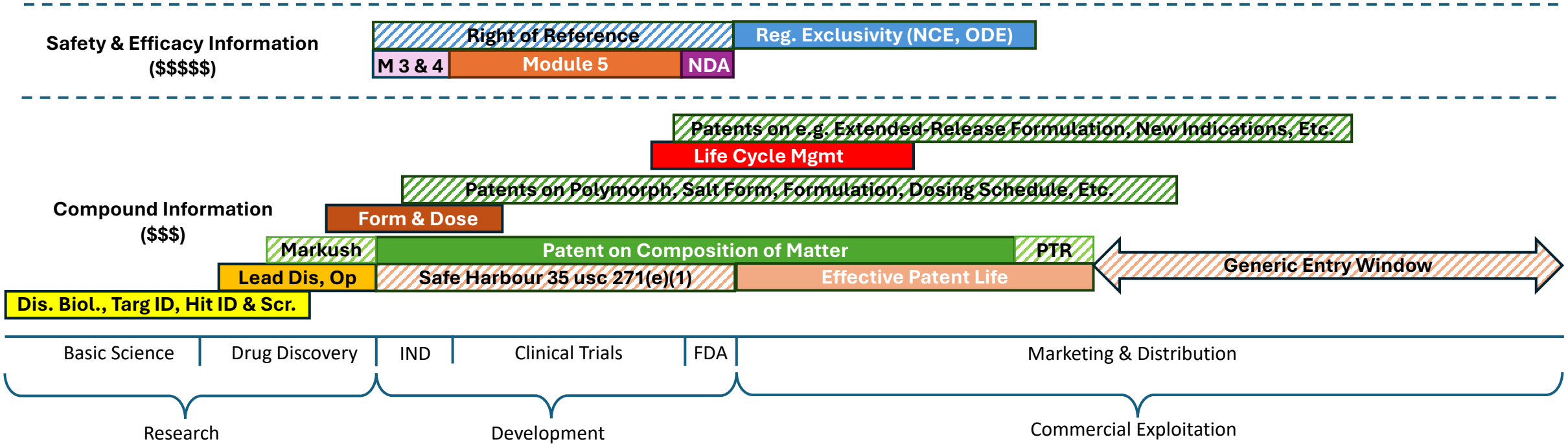


Economics Paradigm

- NPV of investment in discovery science (disease biology, target ID and validation) is highly negative
- Overinclusive
  - Private sector underinvests
  - Public funding and pre-competitive dynamics predominate (norms around publication, attribution, cooperation)
- Systemic inefficiencies
- NPV inflects to positive
- Ineffective
  - Private sector invests in lead compound development & patenting
  - Market failure dynamics predominate (norms around secrecy and duplication, price maximization)

Pharmaco-Statistical Paradigm

- Underinclusive
  - Disease Biology, Target ID
  - Fixed Term
- Overinclusive
  - Markush Claims
  - "Me-too" & Evergreening
- Systemic Inefficiencies
  - Secrecy
  - Duplication
- Ineffective
  - Market failure dynamics predominate (norms around Disease Biology and Target ID, Risk aversion)



WHY DOES MARKET FAILURE MATTER?

7,000+ **rare diseases** (large aggregate burden of disease)

- >90% have ho approved treatment
- Small patient populations limit incentives

May be 10M annual deaths from **AMR pathogens** by 2050

- Limited investment in new antibiotic classes
- Stewardship programs and short treatment courses limit incentives

1B people affected by **neglected tropical diseases**

- Impecunious patient populations limit incentives

Many large indications better understood as groupings of smaller, genetically well-characterized patient populations

VAST HEALTH NEEDS ARE UNDERSERVED BY CURRENT INNOVATION POLICY

OPEN SCIENCE MODEL AS SOLUTION

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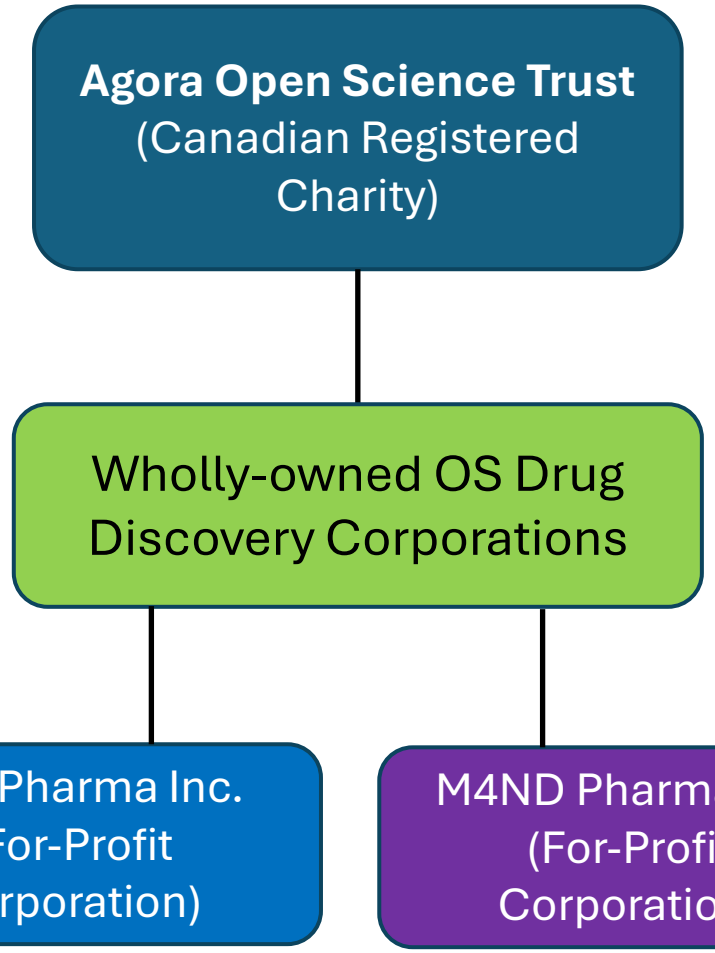
Problem:

- Drug development paradigm reliant on early patenting to attract private investment cannot generate an approved drug for many unmet therapeutic needs – let alone an affordable drug

Solution:

- Reimagine preclinical drug development and clinical proof-of-concept / target validation **for underserved needs (market failures)** as **pre-competitive, mission-oriented science**
- Use open science model in a charitable organizational structure to crowdsource and coordinate **multi-institution cost- and risk-sharing collaborations**, raise **non-dilutive funding**, and **de-risk novel targets** to the point of **investment viability (at affordable prices)**
- Use the organizational structure to hold IND and regulatory dossier, leverage relationships with **academic drug discovery centers** and **clinical trial consortia**, and outsource critical functions to **CROs and CDMOs**
- Ensure **freedom to operate** through ongoing rapid disclosure of 'inventions'
- Engage in **technology transfer** to private sector via investment or commercial licenses at least **after clinical proof-of-concept** using **regulatory dossier as asset** instead of patents → regulatory exclusivity, priority review voucher*
- Negotiate **commitments on access and pricing** with exclusive commercial licensee(s) or **introduce competitive generic supply** (either approach not dictated by private investors return)
- **Rapidly share data** from failed experiments and trials to help others **avoid costly duplication**
- **Reinvest** any proceeds into patient access initiatives and/or other open science projects

Agora Corporate Structure



Corporate structure is able to:

- Maintain project focus on open science and affordable access for patients
- Hire employees and manage project workflows
- Raise and disburse funding from philanthropic, scientific, and industrial granting programs
- Act as regulatory sponsor for drug candidates
- Enter contracts and licenses
- Return net profits (if any) for future charitable use on a tax-free basis

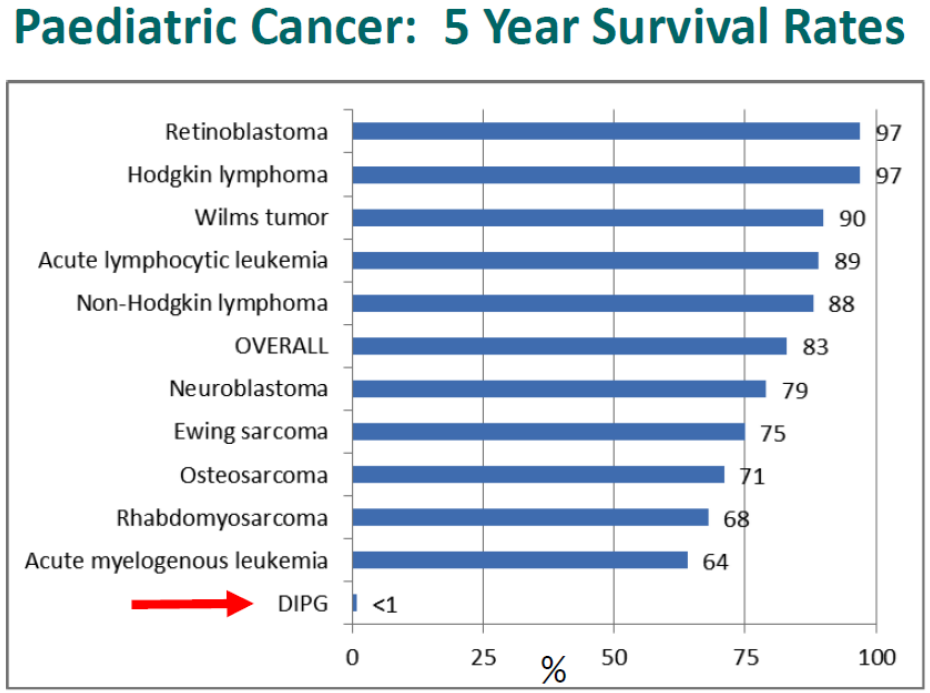
Agora's First M4 Program:

Diffuse Intrinsic Pontine Glioma (DIPG)

DIPG

- Dire therapeutic need
- Mechanistic evidence for a novel target – ACVR1/ALK2
- Novel target is in a known druggable target class (kinases)
- Early enabling data and tools available

BUT: Difficult Investment Case

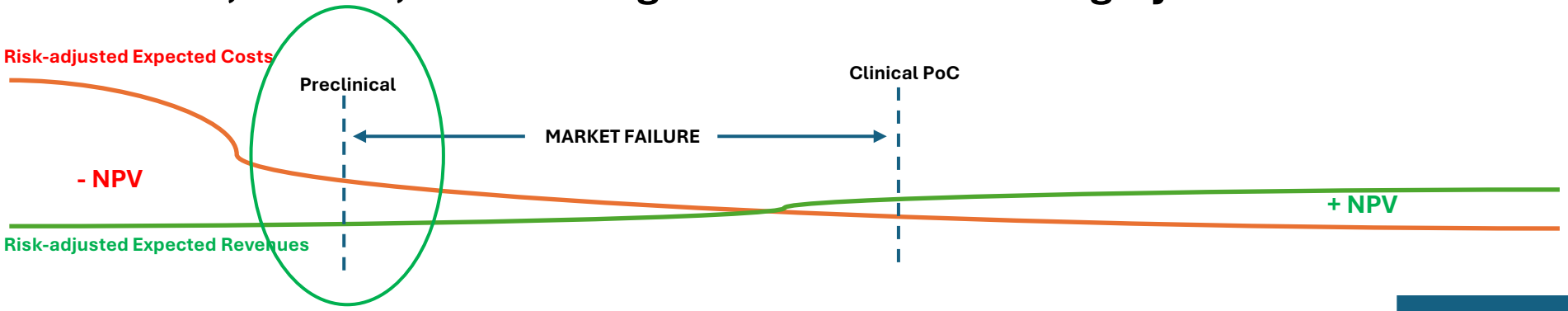


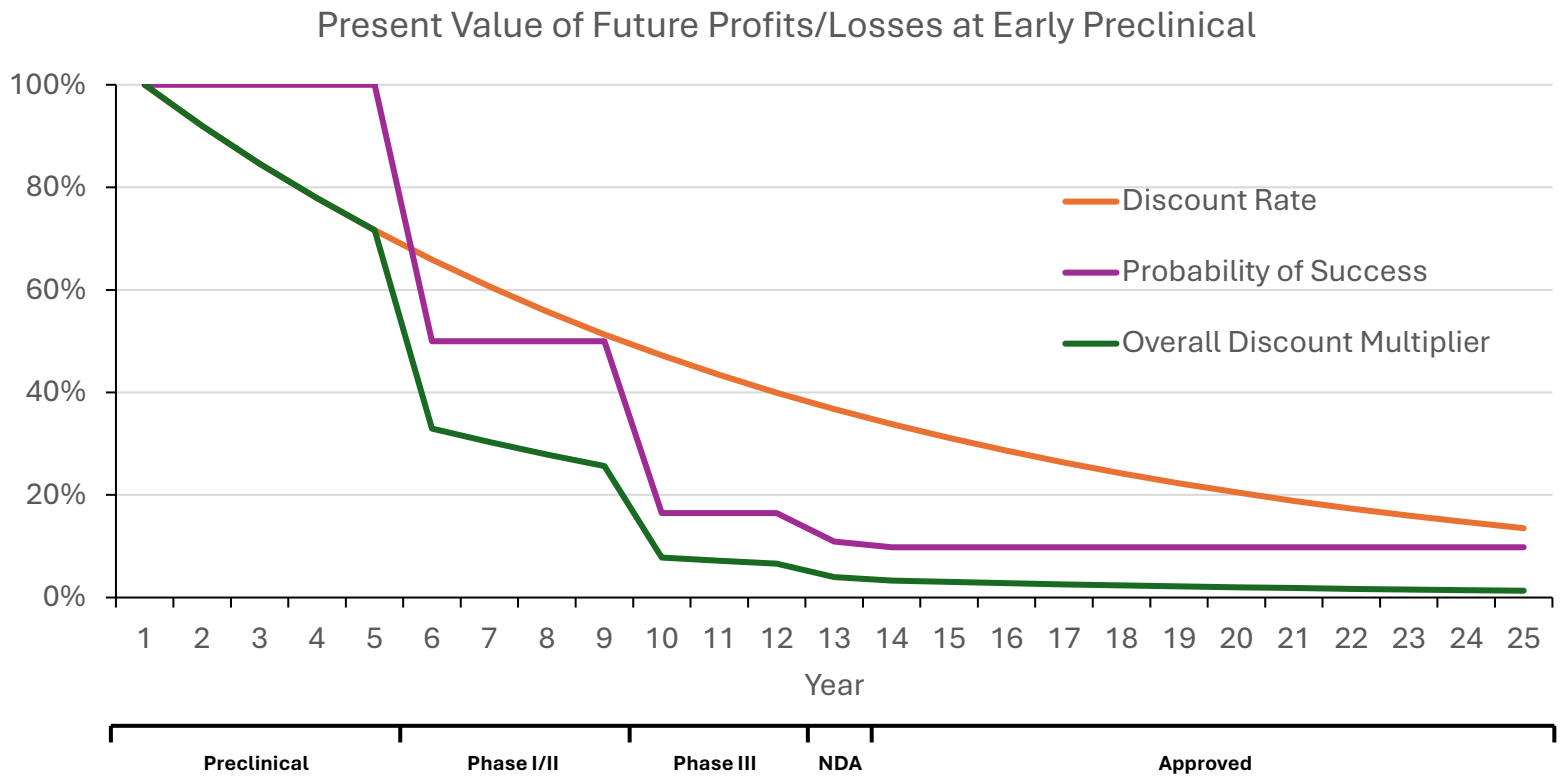
A Diffuse Intrinsic Pontine Glioma–Driving *ACVR1 (ALK2)* Mutation Causes Oligodendroglial Lineage Cell Expansion and Differentiation Arrest

Jerome Fortin[1*], Ruxiao Tian[1], Ida Zarrabi[1], Graham Hill[1], Eleanor Williams[2], Gonzalo Sanchez-Duffhues[3], 3 Midory Thorikay[3], Parameswaran Ramachandran[1], Robert Siddaway[4], Jong Fu Wong[2], Jillian Haight[1], 4 Annick You-Ten[1], Bryan Snow[1], Andrew Wakeham[1], Daniel Schramek[5,6], Alex N Bullock[2], Peter ten Dijke[3], 5 Cynthia Hawkins[4,7,8] and Tak W Mak[1*]

Investor Perspective at Preclinical:

Small, Distant, and Contingent Cash Flows are Highly Discounted at Present Value

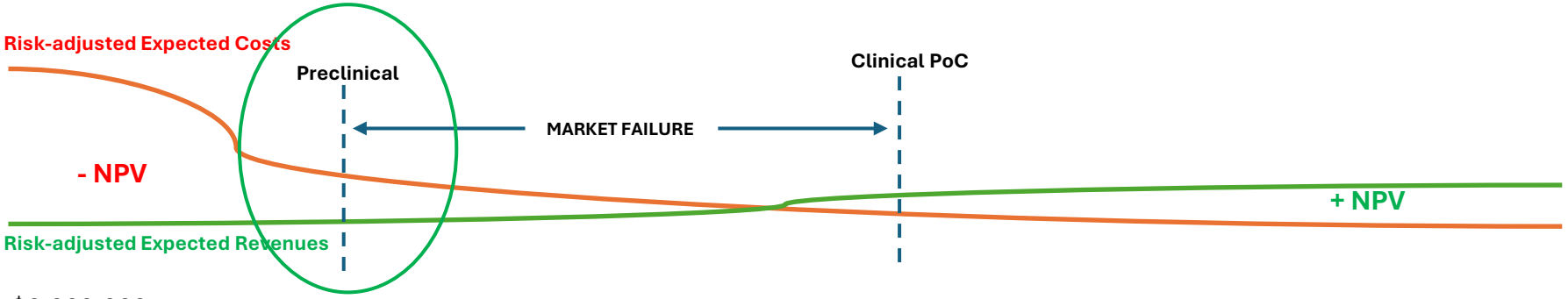


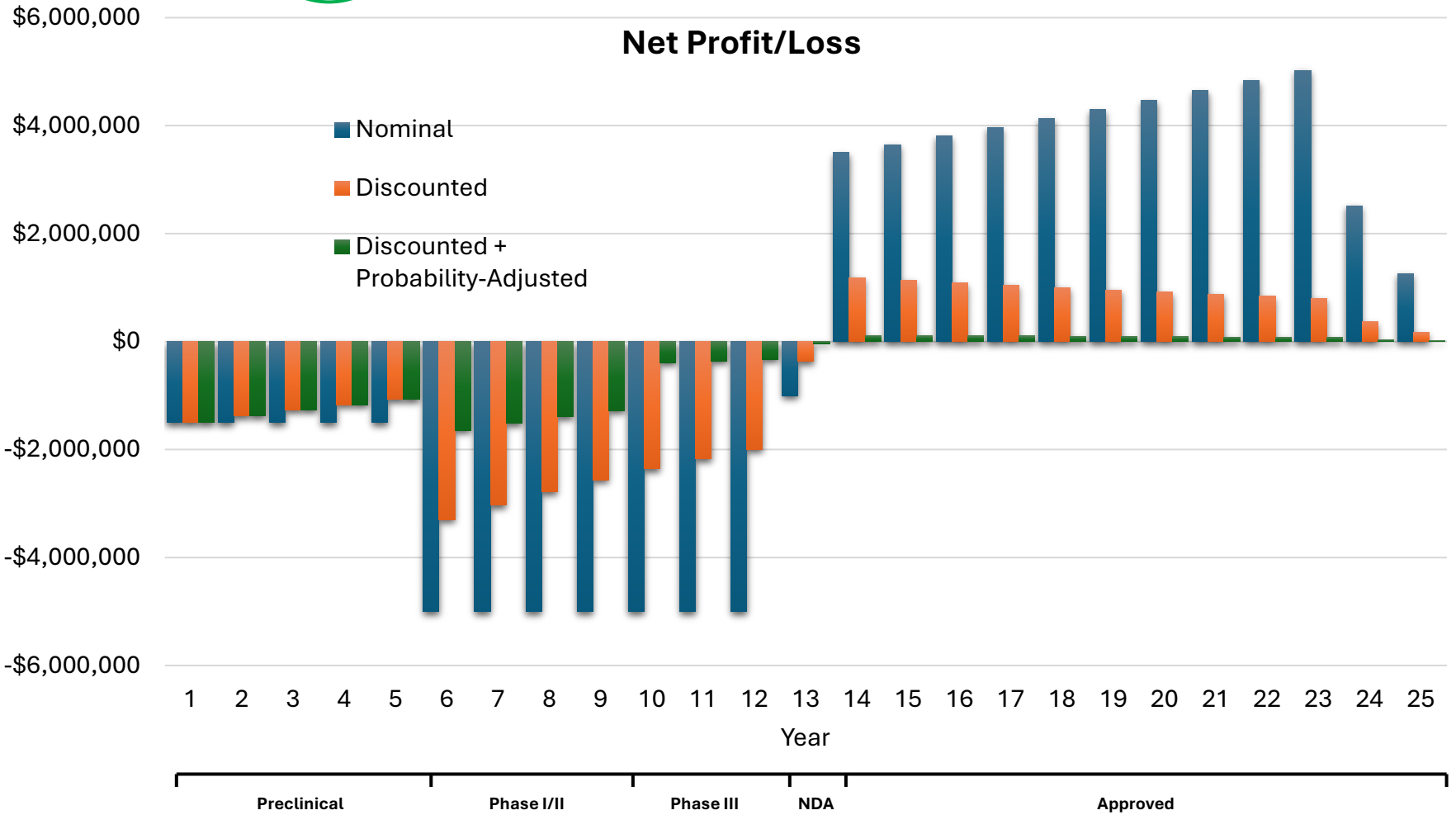


Key Factors
High upfront R&D costs
High probability of failure at each stage
Long lag time to revenues

Very difficult to impossible to model a positive return on investment

DIPG Investment Case at Preclinical for Reasonable Target Price (e.g. $10,000)



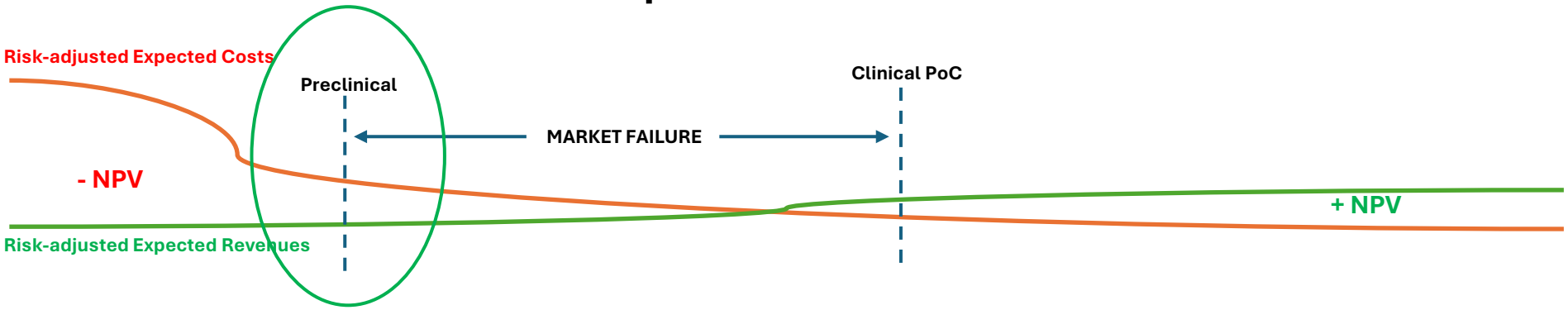


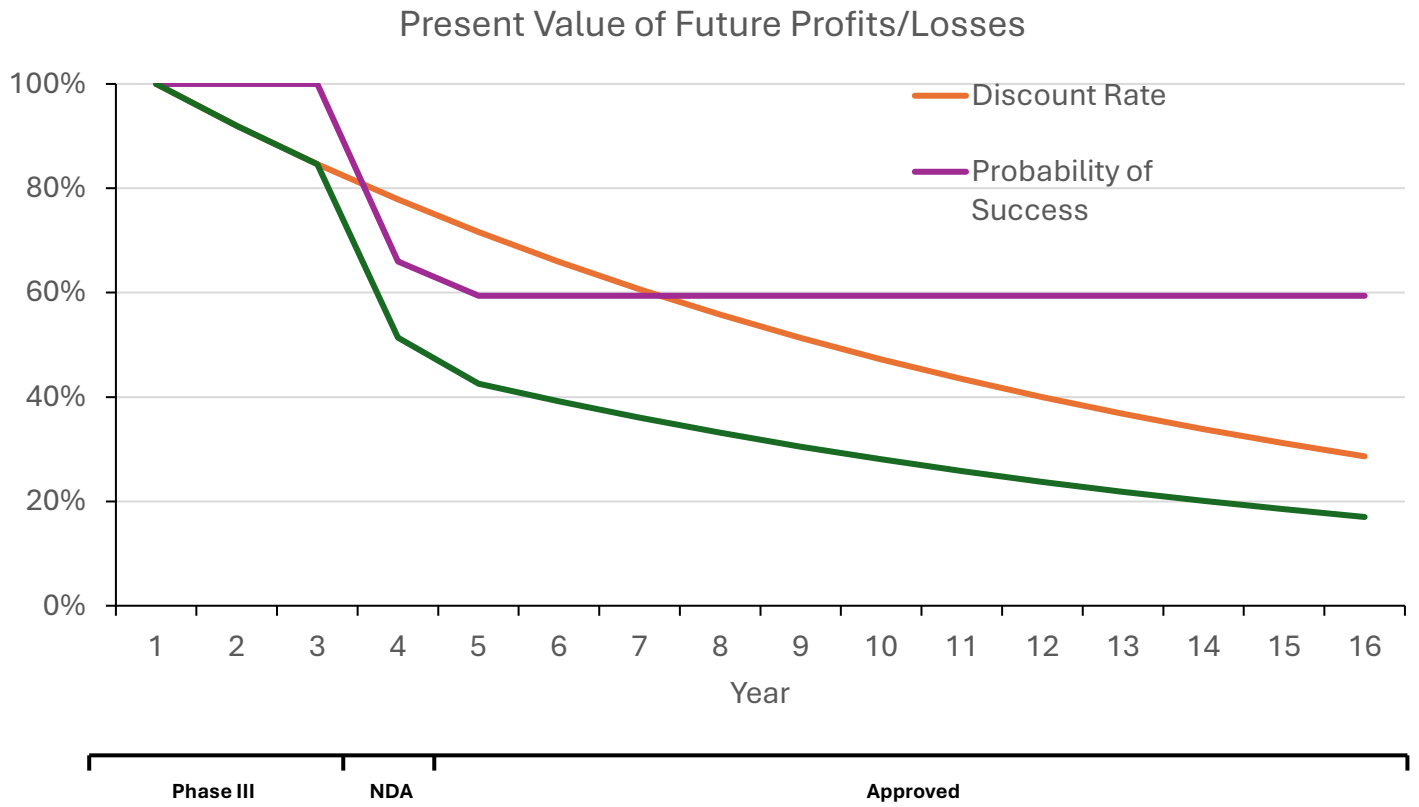
Assumptions and Outcomes	
Investment Decision Point	Preclinical
Probability of Success	10%
DIPG Patients Treated Per Year After Approval	500
Total Projected Investment	$59,625,000
Revenue Per Treatment Course – Year 1	$10,000
Cumulative Nominal Projected Net Profit	$2,587,296
Risk-adjusted Net Present Value	$-12,333,237

***Despite a nominal net profit, there is no commercial incentive to develop this drug.**

Goal: Use Open Science Partnerships to Traverse the Market Failure Gap

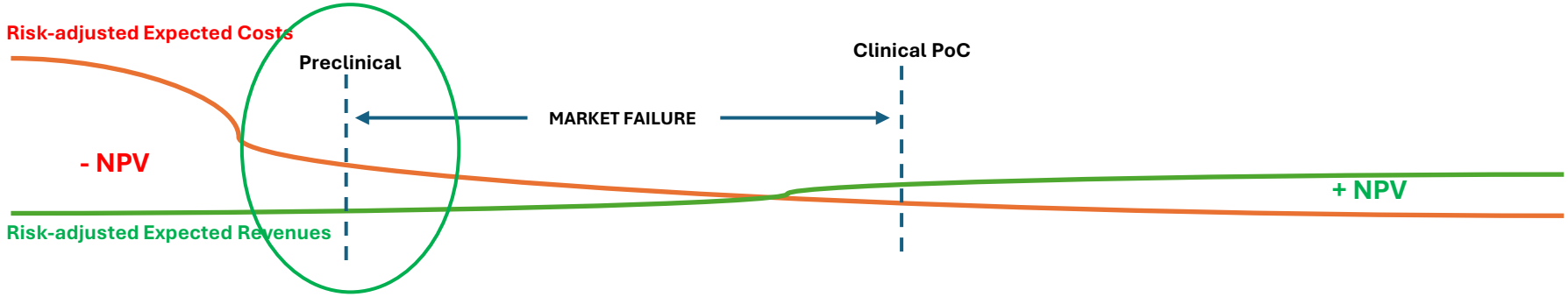
Generate Much Improved Discount Curve / Economics at Clinical PoC

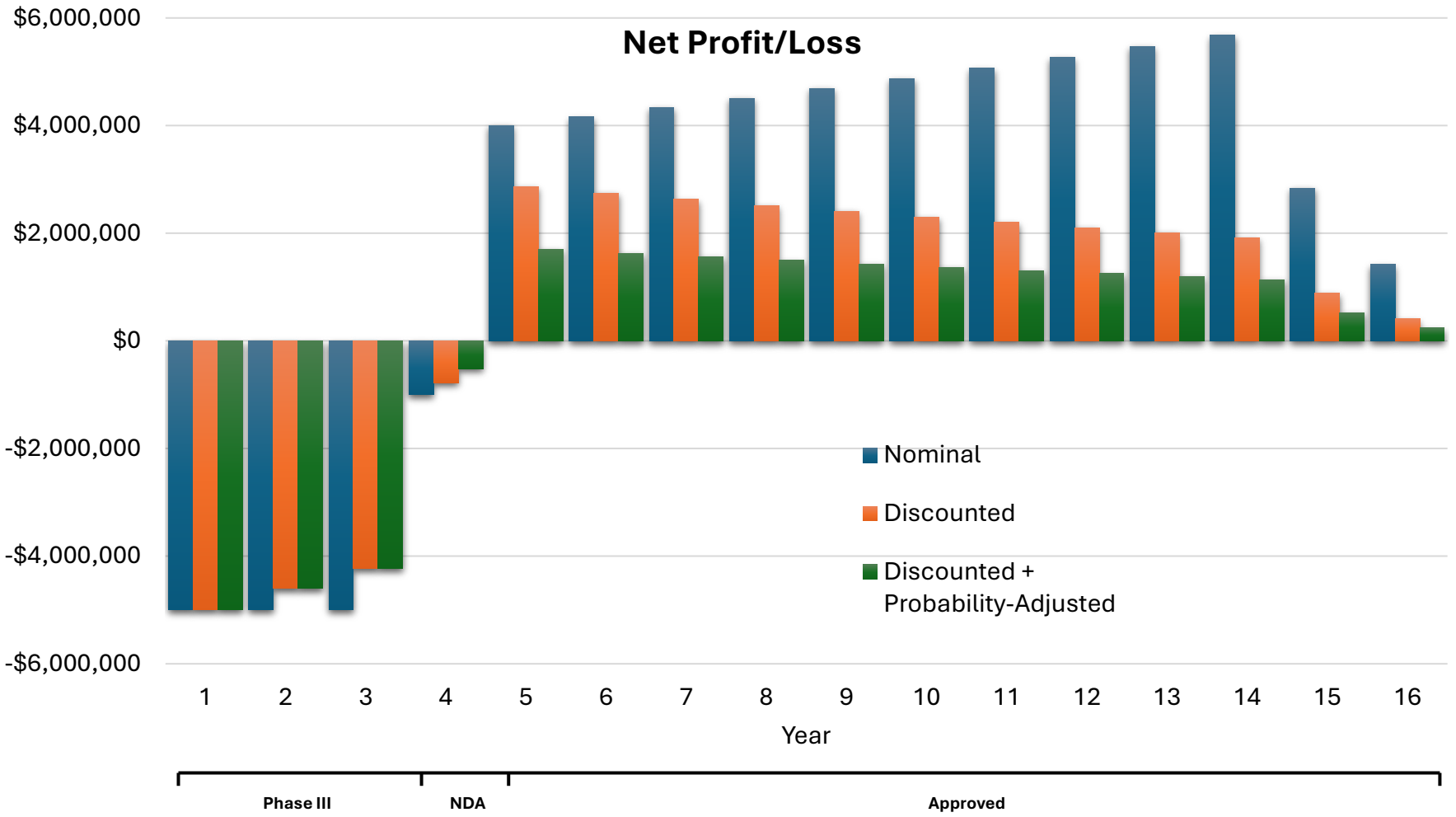




Key Factors
Lower upfront R&D costs
Lower risk of failure
Shorter timeframe to revenues

DIPG Investment Case – Much Improved Economics after Clinical PoC





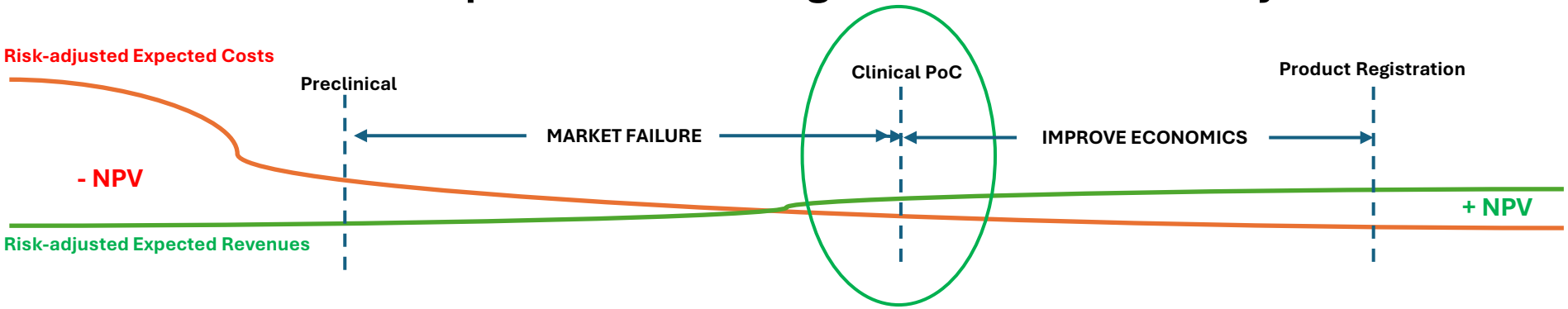
Assumptions and Outcomes

Investment Decision Point	Pivotal trial
Probability of Success	59%
DIPG Patients Treated Per Year After Approval	500
Preclinical through Clinical Proof-of-Concept Funding	Non-Dilutive / No Return of Capital Required
Total Projected Investment	$32,125,000
Revenue Per Treatment Course – Year 1	$10,000*
Cumulative Nominal Projected Net Profit	$36,308,525
Risked-adjusted Net Present Value	$497,565

***Commercial investment for a DIPG drug to be priced at $10,000 per treatment course is economically viable at this stage.**

Ideal: Complete Clinical Trials & Registration without Dilutive Capital

Decouple Manufacturing & Distribution Entirely from R&D Costs



Key Factors
No R&D costs
No risk of failure
Immediate revenues

SUPRACOMPETITIVE PRICING NOT NEEDED

HOLD NDA AND AUTHORIZE ANDA APPLICANTS

AND/OR WAIVE EXCLUSIVITIES

M4K Pharma Progress

A Successful Collaborative Hit-to-Lead Program for DIPG

	Target Product Profile
Potency and Selectivity	
ALK2 enz potency IC50 (nM)	< 10
ALK2 cell potency IC50 (nM)	< 100
DIPG cell lines CC50 (nM)	< 500
ALK5 5 selectivity (cell, fold)	> 500
Kinase selectivity	No relevant kinases > 50% inh @ 1 uM
In Vitro ADME	
MLM T1/2 (min)	> 60
HLM T1/2 (min)	> 60
Caco-2 AB	> 4
Caco-2 BA/AB	< 2.5
Solubility	> 10 uM
CYP inhibition (IC50 or fold)	> 10 uM or >30
hERG inhibition (IC50 or fold)	> 10 uM or >30
AMES	negative
In Vivo ADME	
F%	> 50
Cl (ml/min/kg)	< 25% QH
T1/2	> 6
Dose/exposure	Linear in therapeutic range
Cbrain/Cplasma	> 1
Cmin (brain)u	> 3x DIPG CC50
In vivo efficacy	
Efficacy in mouse xenograft	Reduction in TV; increase in survival
Therapeutic index	No toxicity at therapeutic dose
CNS PD endpoints	pSMAD1; ID1 expression decrease
Peripheral biomarker	Circulating tumour DNA decrease

$2.5M non-dilutive seed funding raised

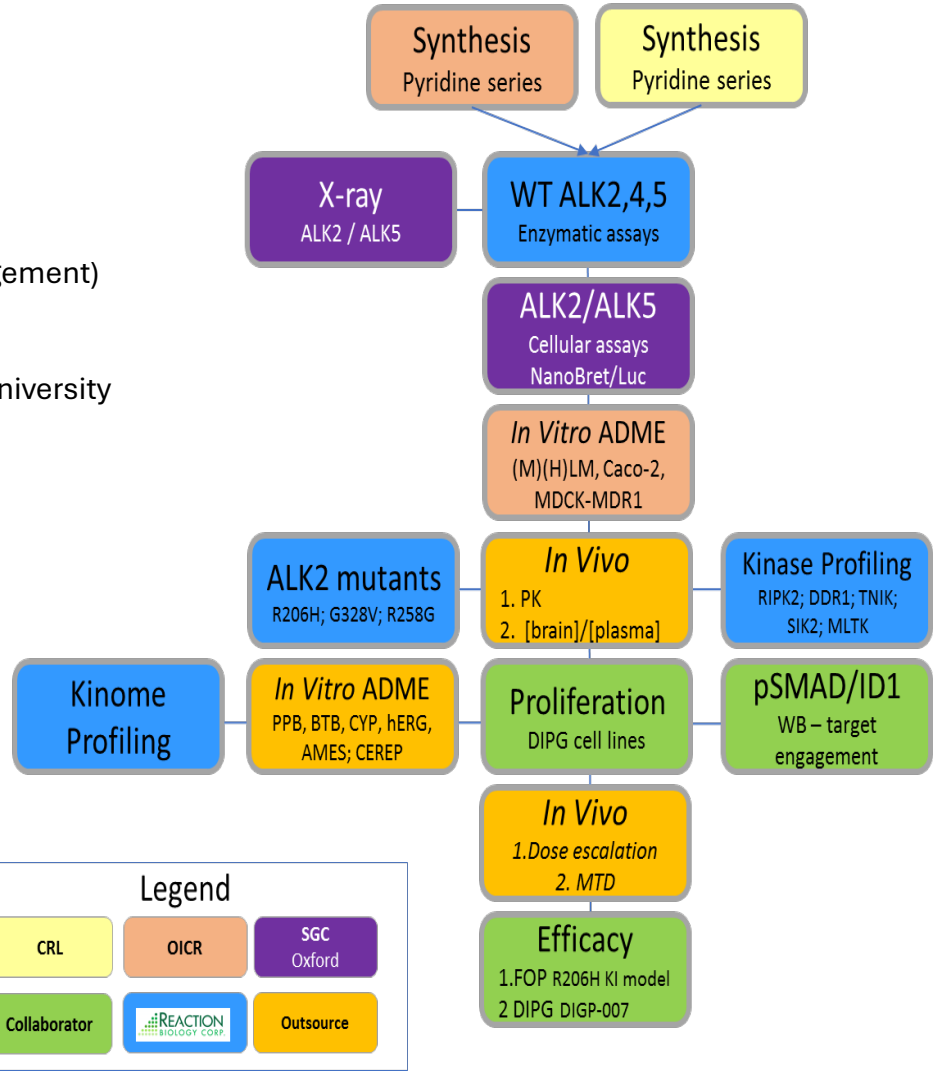
Target product profile and screening cascade designed

Many collaborators provided in-kind scientific contributions

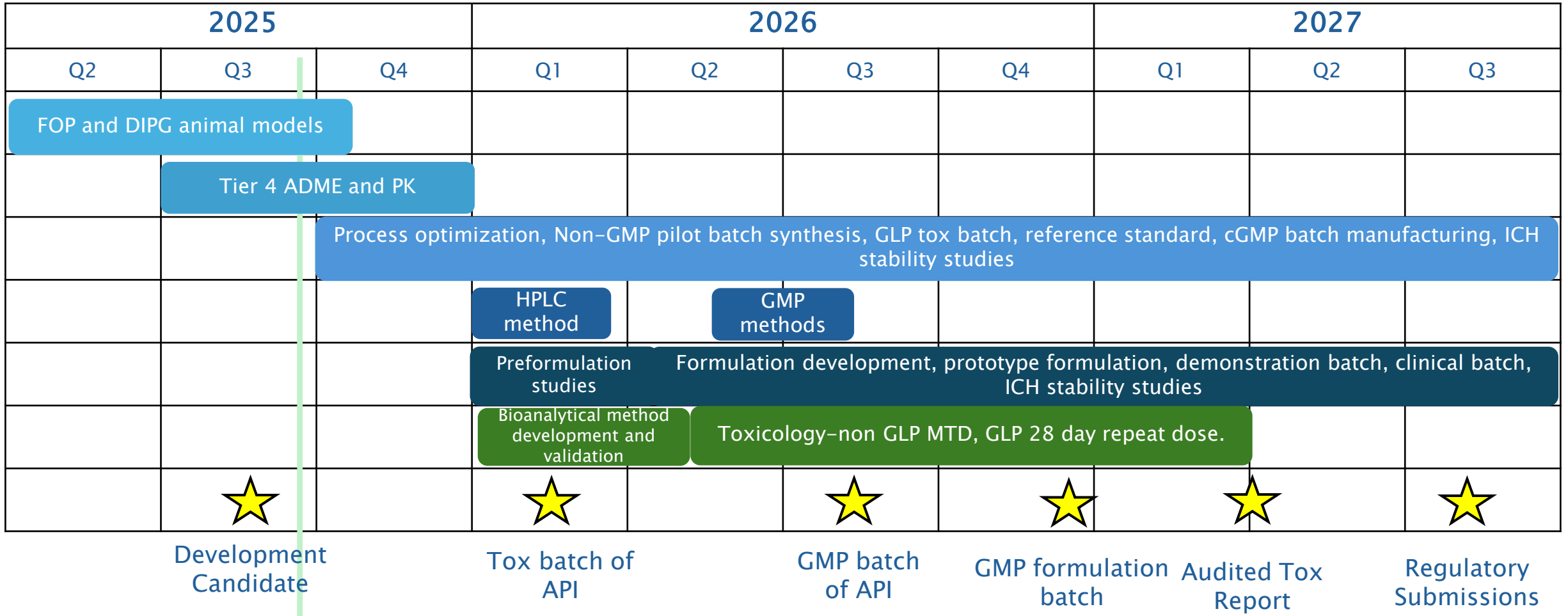
- Ontario Institute of Cancer Research (Med Chem, project management)
- *Charles River Laboratories** (Med Chem, Assays)
- *Reaction Biology Corp** (Assays)
- Structural Genomics Consortium (Structural biology, assays) - University of Toronto, Oxford University, University of North Carolina
- ICR UK (Med chem, *in vivo* PD model)
- Sant Joan de Deu, Barcelona (*in vivo* PD model)
- Tufts University (assays)
- University of Pennsylvania (*in vivo* PD model)
- The Brain Tumour Charity
- Children's National (*in vivo* PK)

Clinical candidate nominated Sep 2025 (M4K2009). $3M+ non-dilutive funding for IND.

***CONNECT Consortium has committed to run Phase I and II trials and provide regulatory support if IND is achieved**



Next Steps: IND-Enabling Timeline



Milestone

Target CTA/IND Submission Q3 2027

WHAT BENEFITS ACCRUE TO US USING OPEN SCIENCE?

- **Benefits to our program**
  - Rapid data sharing and pre-competitive, mission-oriented ethos have enabled us to crowdsource inputs, collaborate broadly, and advance our program without a large pot of centralized funding
    - Crowdsourced inputs have included: funding, know-how, med chem, biophysical assays, cell assays, in vitro and in vivo ADME/DMPK, human cell lines, animal models, clinical trial expertise
  - Commitment to open science has been normatively attractive to public and philanthropic granting bodies, academic & *industry* collaborators, and patients
    - Public funders want to ensure work they support has maximal benefit across their research priorities
    - Scientists and clinicians are motivated by unencumbered ability to publish and contribution to the public good
    - Industry participants are motivated to showcase or validate assets or services openly, engage in corporate social responsibility, gain early access to new and/or tacit knowledge
    - Patient groups want to ensure patient trial participation has maximal impact
  - Rapid disclosure of chemistry creates freedom to operate
  - Open clinician and patient advocate input into trial protocols and analysis plans can improve trial design and engender trust in patient communities to participate in trials

- **Spill over benefits (positive externalities)**
  - Reduces redundancy, duplication & patient harm -> more shots on goal with the same $$$
  - Transparency improves reproducibility & public trust in scientific work
  - Enables secondary analysis, meta-analysis, and new hypothesis generation
  - Improves decision-making by regulators, HTAs, payors, prescribers, and patients
  - Formation of new knowledge networks generates economic activity

WHY DON'T WE USE PATENTS?

FOR EXAMPLE, WE COULD PATENT AND IMPLEMENT AN OPEN OR PUBLIC INTEREST LICENSING APPROACH

BUT

THE PURSUIT OF PATENTS MAKES IT HARDER FOR US TO EFFICIENTLY ALIGN LIMITED RESOURCES ACROSS INSTITUTIONS

- Preserving patentability requires a **period of secrecy** that excludes anyone not under **NDA** and/or that hasn't signed an (often complex) **IP agreement** (re possibility of distributed inventorship)
  - **Transaction costs** rise significantly with larger collaborations -> negotiation costs, delays, failures to agree, governance complexity
  - **Undermines rapid data sharing and crowdsourcing of inputs**

- Pursuing patents introduces an **ownership/property mindset** along with **motives for control and compensation** that undermine collective action
  - Alternative motives can predominate in **IP-free zones of production** -> e.g. open-source software, norms of academic science, SGC programs

- **Obtaining** patents is **very costly** and **diverts scarce time and resources** away from research & development

- **Monitoring** for patent infringement by third parties and **enforcing** patent rights is **extremely costly**

- Existence of patents can **deter follow-on innovation**, lead to spill-over costs that we want to avoid

Why Are We Focused on Regulatory Exclusivities?

FOCUSING ON THE PRECLINICAL AND CLINICAL REGULATORY DOSSIER AS OUR PRIMARY COMMERCIAL ASSET GIVES US THE PRINCIPAL BENEFITS OF PATENTING WITHOUT UNDERMINING OUR OPEN SCIENCE APPROACH

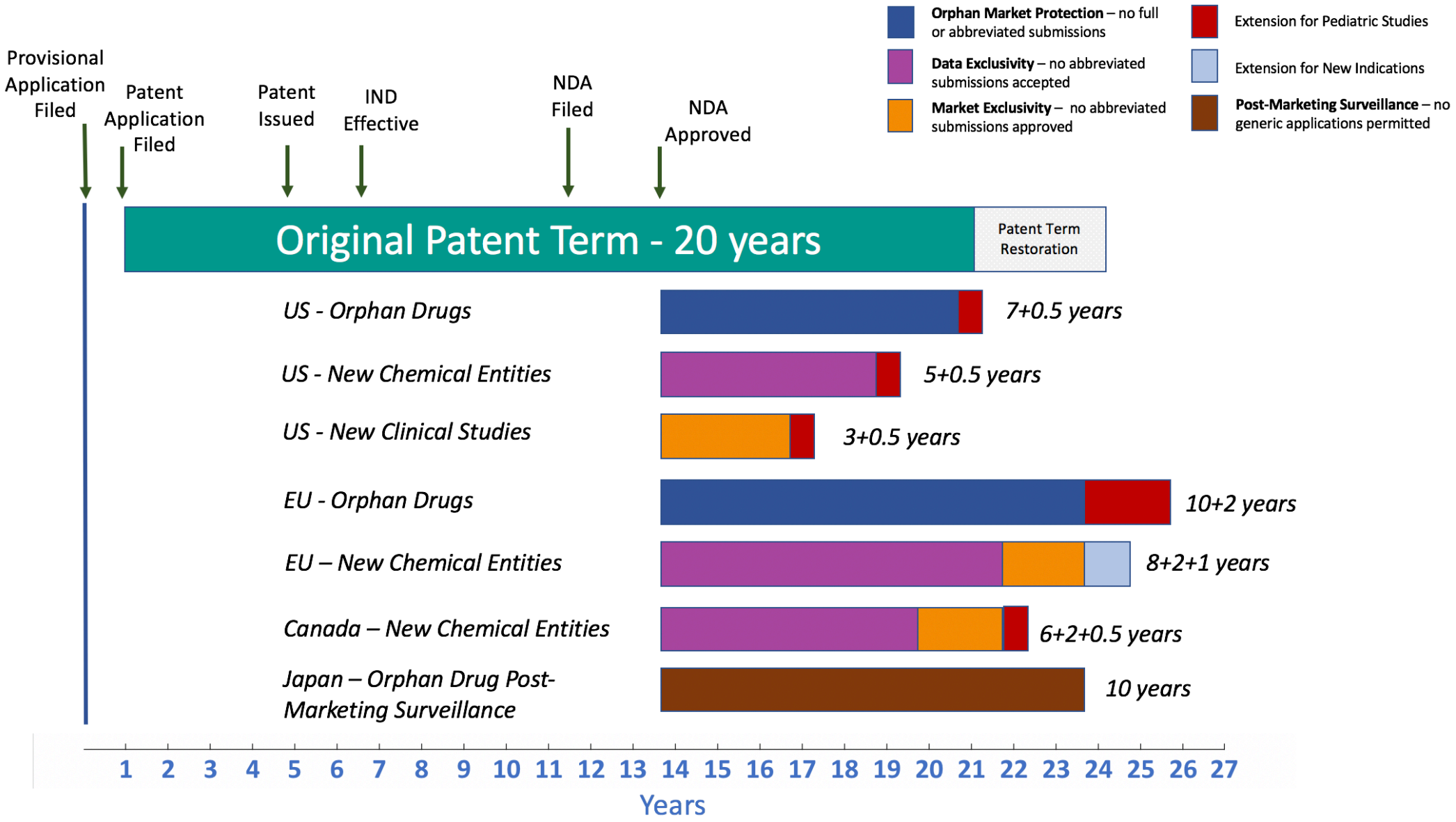
Regulatory exclusivities more directly **preempt freeriding** by competitors on pharma's primary R&D investment – safety & efficacy data – to forestall generic entry, without patent system pathologies:

- **More consistent with open science:** not predicated on prior secrecy -> not invalidated by prior disclosure / sharing / open collaboration
- Don't need to entail significant **transaction costs** in early up-stream discovery – greatly simplifies initiation and governance of open collaborations
- Virtually **costless** to obtain and enforce
- **Not subject to gaming** by sponsors (evergreening)
- **Not subject to challenge** by competitors
- Provide a period of market protection that is **certain *ex ante*** regardless of development timelines
- Don't encumber **follow-on research**

Sponsors **do not need a patent** (composition of matter or otherwise) to gain regulatory exclusivity protection

- A primary reason for introducing NCE via **Hatch-Waxman Act** was to induce firms to invest in generating safety & efficacy data for compounds with no patents
- In areas of market failure, **no preclinical investment case** to develop a compound regardless of patent
    - If there is, it is because of the possibility of extreme pricing, so **attempts to impose pricing conditionalities will not be acceptable** to the licensee
    - **Switching costs low** re: counterfactual is to develop and advance different chemistry to avoid patent
- Fast forward to **Phase II PoC or beyond**
    - Potential licensee faced with an advanced regulatory dossier has stronger incentive to invest and negotiate
    - **Switching costs very high** regardless of patent re: counterfactual is to start over by replicating expensive trials
- Many products in the **Orange Book** have NCE and/or ODE but no composition of matter patent (old compounds, naturally occurring compounds, etc)
    - 21 NCEs in current 2025 Orange Book with no patents (13 with concurrent ODE), 22 additional ODEs with no patents
- In light of this dynamic, the substantial costs associated with patenting are not warranted in our programs

Regulatory Exclusivity as Primary Market Asset



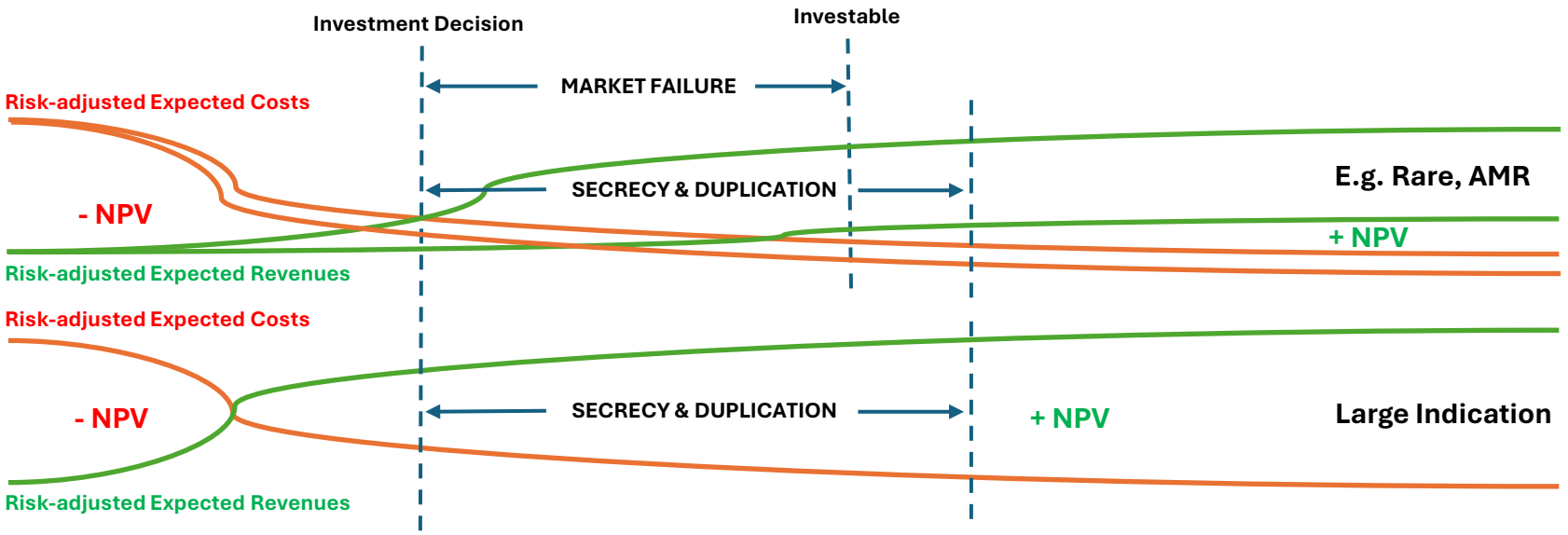
M4K Pharma Regulatory Strategy

- Approval for DIPG Indication
  - **Canada**
    - 6+2 Data and Market Exclusivity period for Innovative Drug (NCE) approval
    - Pediatric Extension for submission of pediatric trials to Health Canada
  - **United States**
    - Orphan Drug (OD) Exclusivity
    - Concurrent New Chemical Entity (NCE) Exclusivity
    - Pediatric Extension of OD and NCE depends on FDA Written Request process
    - Rare Pediatric Disease Priority Review Voucher (if extended by Congress)
  - **EU**
    - Orphan Drug Exclusivity + Pediatric Extension for compliance with EMA Pediatric Investigation Plan (PIP)
    - Concurrent 8+2 Data and Market Exclusivity period for NCE
  - **Japan**
    - Post-Marketing Surveillance period = prohibition on generic submissions

What about pre-approval competitive dynamics?

- Regulatory exclusivities start **after approval** but project progress and social utility maximized by earlier data sharing and collaboration.
- What about competitors **freeriding on data before approval?**
  - **"Right of Reference"** for NDA exclusive to sponsor ***prior to*** regulatory approval – enables data disclosure without regulatory use authorization
  - 505(b)(2) literature-based marketing applications (SRTDs in Canada) impeded by **absence of substantial prior marketing experience** and **inability to complete bridging studies**
  - Bolster with **data access license** that prohibits competitive regulatory use (e.g. **EMA portal**)
  - **Patient-level data** cannot be shared for ethical reasons but regulators may require audit rights
  - Applicant using third party data **not eligible for regulatory exclusivities** (deterrent)
- What about competitors **racing to market with their own NDA packages?**
  - **Investment case absent at preclinical** in areas of market failure + **absence of patent** deters typical commercial actors from investing
  - At **clinical proof-of-concept** -> investment case may be strong, but **too late and costly** to play catch up with independent preclinical and clinical studies
  - Prospect of competing OS program bringing **low-cost version** to market reduces potential upside
- **Policy intervention** should address gaps to incentivize more firms to participate in open drug development programs, including for larger indications

Voluntary Innovation Policy 'Carrots'



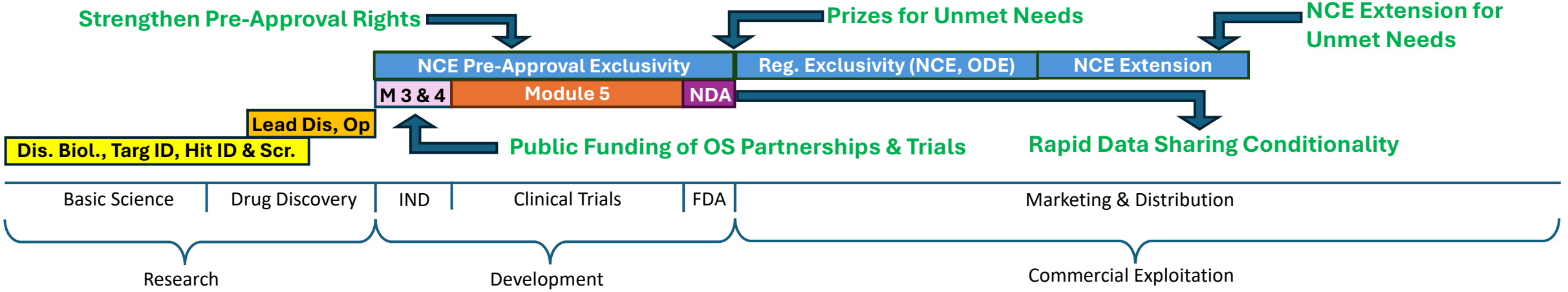
Impose conditionalities on these targeted market failure incentives:

- Forego patents
- Cost transparency and price cap

Avoid introducing more secrecy & duplication:

- Condition these incentives on rapid data transparency
- Host open data infrastructure

Consider rapid data transparency obligation for existing regulatory exclusivities to further eliminate secrecy & duplication



PRVs as Prizes for Addressing Market Failure?

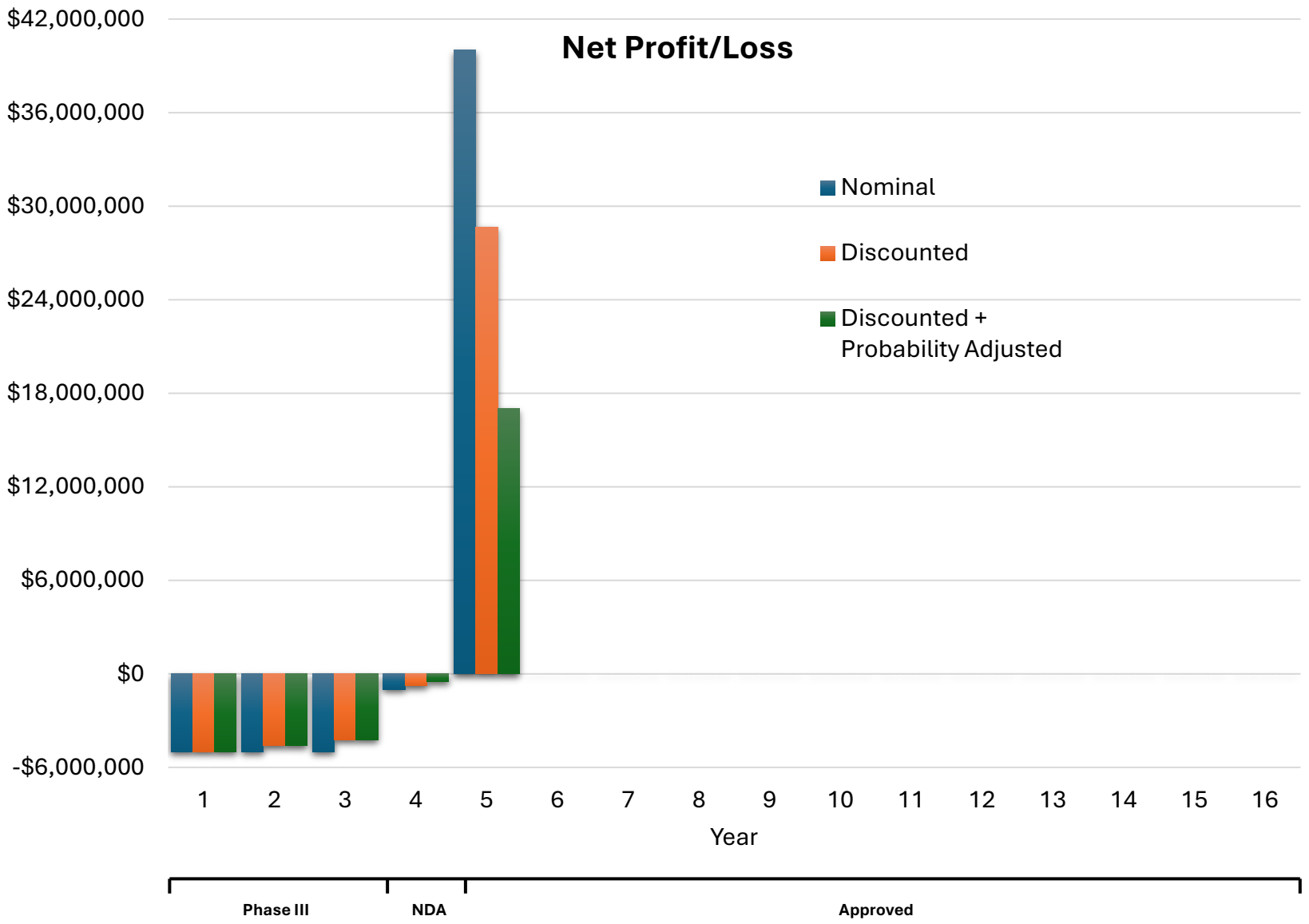
Priority Review Vouchers as ‘Prizes’

- FDA approval of drug for rare pediatric disease → sponsor receives voucher for priority review of a different product
- **53** rare pediatric disease PRVs awarded from beginning of program (2012) to April 30, 2024.
- Voucher may be sold to another sponsor – current market value approx. **$100M USD**
- Could M4K raise sufficient capital by offering investors the right to a **tranche of a future PRV sale as a Prize?**
- Program will sunset in 2026 without further Congressional action
- (EU has recently tabled concept of Transferable Exclusivity Vouchers in AMR)

Approach could help enable complete **decoupling of marketing & distribution economics from R&D costs**

- M4K could hold the NDA and launch the product ‘straight to generic’ through multiple authorized generic licensees

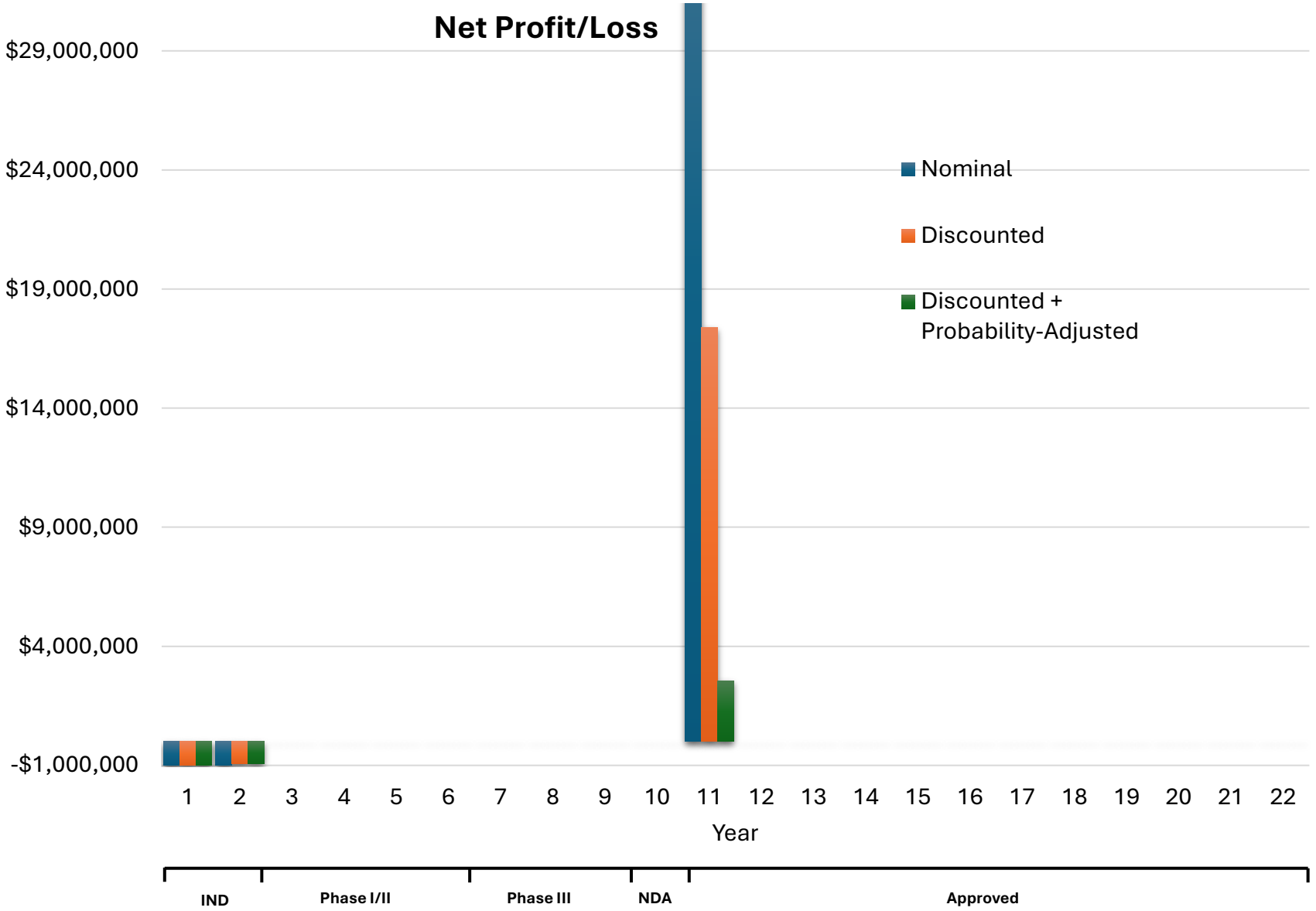
Investor after Clinical PoC with PRV and ‘Straight-to-Generic’ Approach



Assumptions and Outcomes	
Investment Decision Point	Pivotal trial
Probability of Success	59%
DIPG Patients Treated Per Year After Approval	500
Total Projected Investment	$16,000,000
PRV Sale Allocation to Commercial Partner	40% ($40,000,000)
Marketing and Distribution	Authorized Generics
Nominal Net Profit	$24,000,000
rNPV	$2,675,563

*Approx minimum required to generate positive rNPV

IND Stage Investment for Tranche of PRV Sale (e.g. first $40,000,000)?

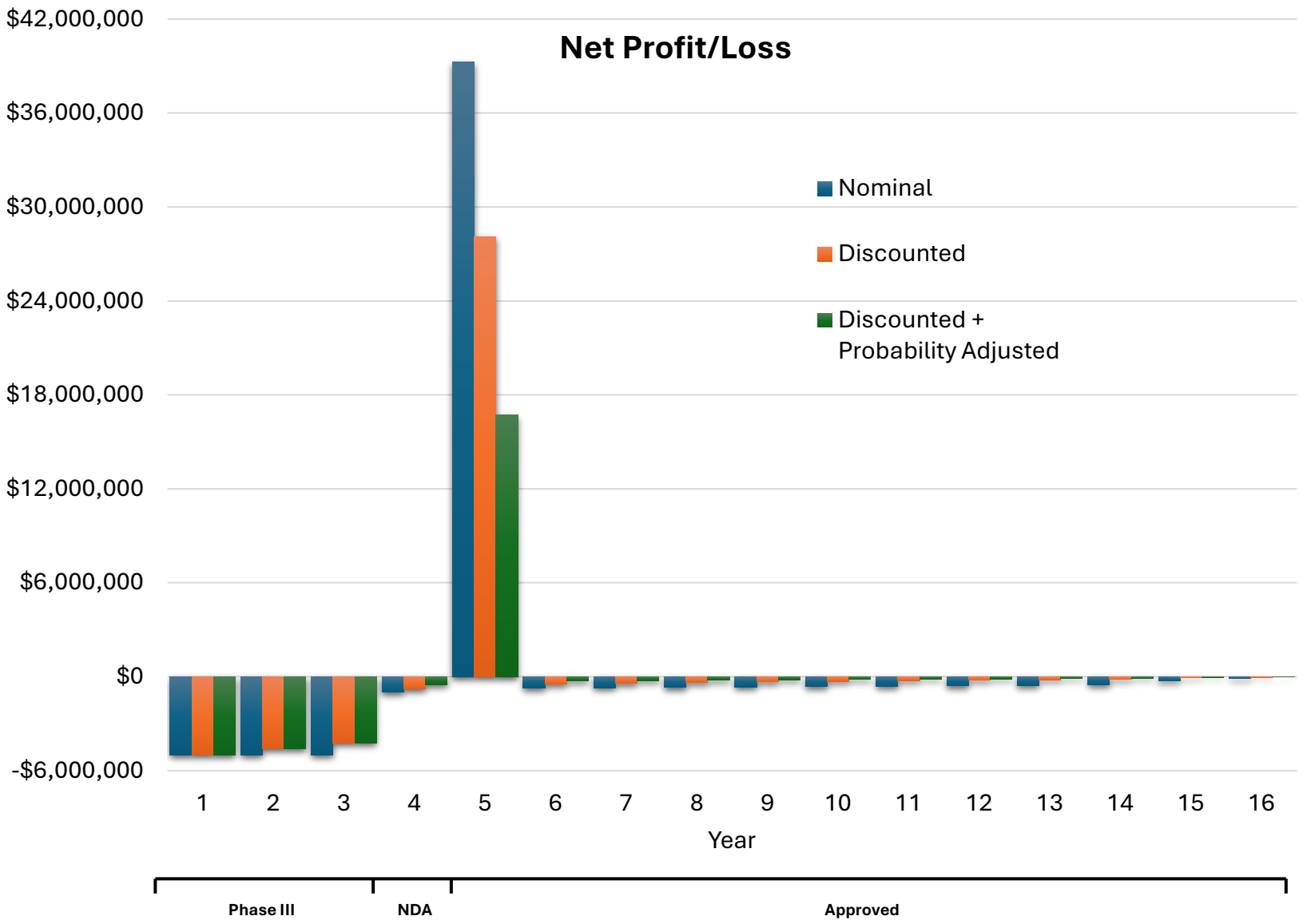


Assumptions and Outcomes	
Investment Decision Point	IND
Probability of Success	15%
Total Investment Required	**$2,000,000**
Right to First Tranche of PRV Sale	**$40,000,000**
Nominal Projected Net Profit	**$38,000,000**
Risked-adjusted Net Present Value	$634,465

***Preserves option to enter commercial partnership later in development.**

***Large potential investor payout multiple could undermine public good motives**

DIPG Investment – Commercial Partner after Clinical PoC with PRV



Assumptions and Outcomes	
Investment Decision Point	Pivotal trial
Probability of Success	59%
DIPG Patients Treated Per Year After Approval	500
Total Projected Investment	$32,125,000
PRV Sale Allocation to Commercial Partner	40% ($40,000,000)
Revenue Per Treatment Course to Commercial Partner	$1,500*
Nominal Net Profit	$17,206,844
rNPV	$627,350

***Approx minimum required to generate positive rNPV**
***Option to Escrow PRV payout to ensure pricing and access compliance**

Contact

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THANK YOU

BACKUP SLIDES

Proposal: Extend C.08.004.1 Innovative Drug Status by 4 Years

- Condition 1: Data from preclinical and clinical studies made available for research use within specified period
  - Reduces R&D redundancy; improves reproducibility and public trust
  - More rapid secondary and meta-analyses, new hypothesis generation
  - Input to HTA and reimbursement decision-making; improves knowledge base for prescribers and patients.
- Condition 2: No patents on medicine; submission of patent list precluded; patent suits waived
  - Enhances the public domain and precludes evergreening tactics
- Condition 3: Price ceiling based on cost effectiveness in HTA or independent pharmacoeconomic analysis
  - E.g. CADTH; Leeway for HC to develop Guidance
  - Improve system uptake and access for patients; reduce financial burden

Proposed Mechanism

- Submission of information or certification to Minister
  - (4.1)(a)-(c)
- Ministerial determination of compliance at 6 years
  - (4.1)(d)
- Extension revoked if Minister later determines that compliance has ceased
  - (5.1)(a)-(c)
- Minister granted authority to require relevant information and documents
  - (5.1)(d)

The Minister Has Statutory Authority

- *Canadian Generic Pharmaceutical Assn. v. Canada (Minister of Health)*, 2010 FCA 334
  - Parliament has broad power to delegate to Governor in Council within enabling legislation (para. 63)
  - "Very broad latitude" to enact regulations Governor in Council "deems necessary" to implement s. 30(3) of Food & Drugs Act (NAFTA, TRIPS) (para. 64, 85)
  - Unless "bad faith", Courts will not second guess Governor in Council's means to implement
  - Not limited to trade secrets; instead protects against "unfair commercial use" of data created by innovators (para. 73-74)

The Minister Has Statutory Authority

Other sub-sections of s. 30 of the Food & Drugs Act

30(1) The Governor in Council may make regulations …

(r) respecting marketing authorizations, including establishing the eligibility criteria for submitting an application

(1.2)(a) respecting the issuance of authorizations … [for] the … sale … of a therapeutic product

(1.2)(b) authorizing the Minister to impose terms and conditions on [such] authorizations

(1.2)(d.1) specifying the business information obtained under this Act in relation to an authorization … that is not confidential business information.

The Minister Has Constitutional Authority

- *Canadian Generic Pharmaceutical Assn. v. Canada (Minister of Health)*, 2010 FCA 334
  - Pith and substance of C.08.004.1: market protection exists "to encourage the development of new drugs, which … constitutes a valid public health and safety purpose" (para. 113)
  - This is a valid exercise of federal criminal law power under 91(27) of the *Constitution Act*
    - "The scope of the federal power to create criminal legislation with respect to health matters is broad, and is circumscribed only by the requirements that the legislation must contain a prohibition accompanied by a penal sanction and must be directed at a legitimate public health evil" (para. 119)
  - Food & Drugs Act s. 31 creates an offence if a person sells or advertises a new drug without authorization

Other Economic Benefits of Open Science

- **Firms participate and invest** > local knowledge hub formation
  - Gain access to tacit knowledge/know-how and talent/expertise
  - Influence research priorities
  - Reduce internal research costs / solve problems common to an industry / share risk
  - Generate freedom to operate
  - Corporate social responsibility / employee morale
  - **Showcase or validate assets or services openly*** – e.g. Charles River, Enamine, Variational

- Local **skills acquisition**
  - Talent and information flow between academia and industry
  - Improves training and creates a local skilled workforce

- **Further commercial opportunities**
  - **Epiphyte3** – lab equipment for protein expression and analysis
  - **1DegreeBio** – antibody and reagent search engine and marketplace
  - Sprint Biosciences – fragment screening
  - Crelux – protein-compound co-crystallization
  - **Custom Biologics** – protein production
  - Promega – reagents
  - Reaction Biology – assays

Current Team

Staff

Peter Sampson, *Agora VP Drug Development* – expert in preclinical and clinical translation of kinase inhibitor oncology programs

Max Morgan, *Agora CEO* – expert in IP, legal, and regulatory frameworks for open drug development / non-profit governance and management

Sofia Melliou, *Agora Communications* – expert in scientific communications

Board of Directors

Aled Edwards, *Agora Board Chair* – expert in pioneering, funding, and executing industry-academic open science partnerships to advance drug discovery

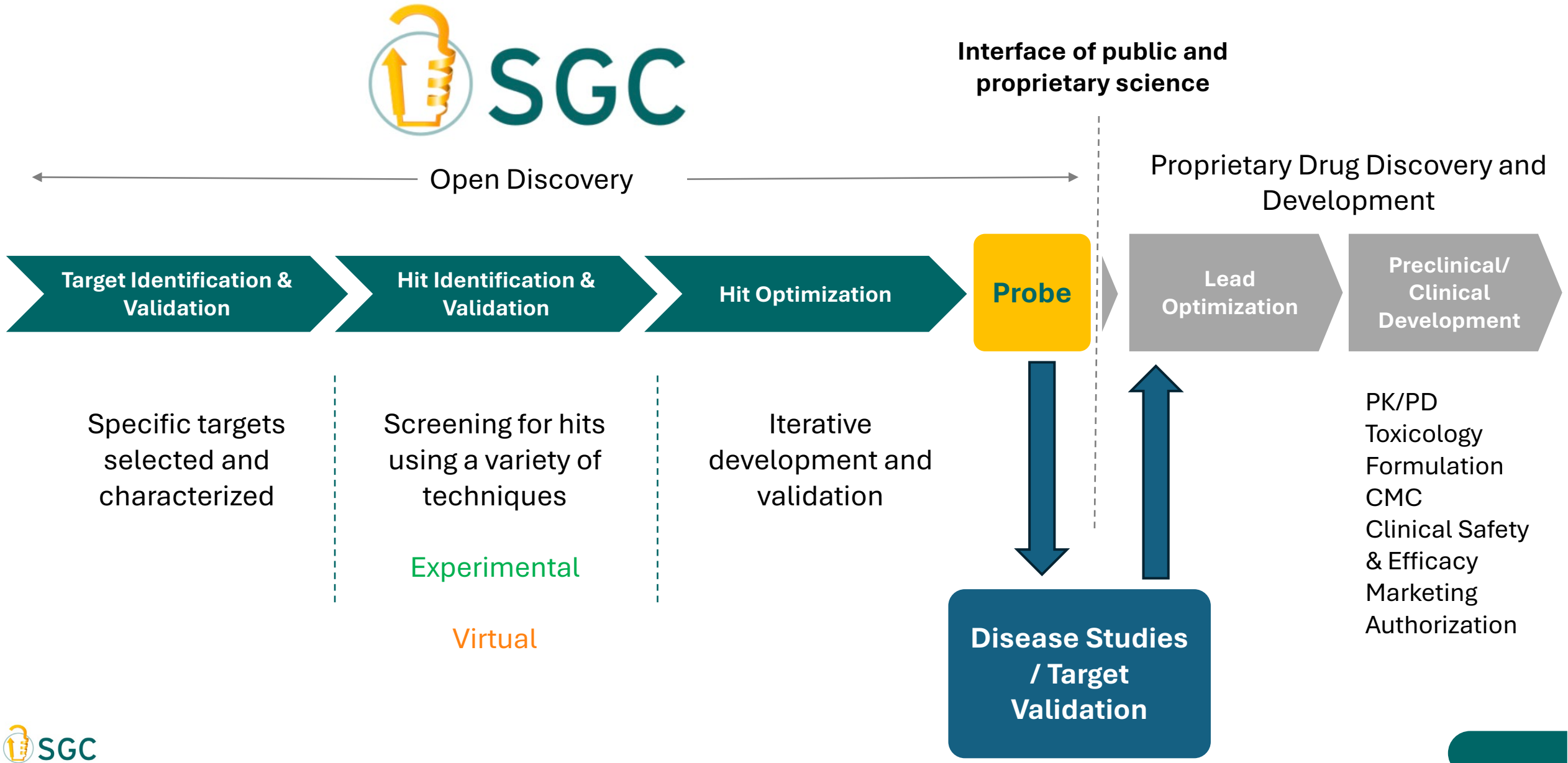
Els Torreele, *Agora Director* – expert in leading access to medicines initiatives

Kate Williams, *Agora Director* – expert in non-profit funding and management of neuroscience research programs

Steering Committee

Member	Title/Affiliation	Role
Peter Sampson, PhD	VP of Drug Discovery and Development/ Agora Open Science Trust	Chairperson
Max Morgan, JD	CEO/ Agora Open Science Trust	Agora Representative
Aled Edwards, PhD	CEO/ Structural Genomics Consortium	SGC Representative
David Drewry, PhD	Principal Investigator/ Structural Genomics Consortium at UNC	SGC Representative
Rima Al-awar, PhD	Head of Therapeutic Innovation and Drug Discovery/ Ontario Institute for Cancer Research	OICR Representative
David Smil, PhD	Principal Scientist/ Ontario Institute for Cancer Research	OICR Representative
Methvin Isaac, PhD	Principal Scientist/ Ontario Institute for Cancer Research	OICR Representative
Charlotte Hardy, PhD	Director/ Charles River Laboratories	Charles River Representative
Kim Hirst, PhD	Group Leader/ Charles River Laboratories	Charles River Representative
Emily Murrell, PhD	Staff Scientist/ Centre for Addiction and Mental Health	CAMH Representative
Chris Jones, PhD	Professor/ The Institute for Cancer Research	ICR Representative
Kate Williams, PhD	Scientific Director/ Krembil Foundation	Krembil Foundation Representative
Owen Roberts, CFA	CEO/ Centre for Probe Development and Commercialization	Independent Business Expert
Jason Karamchandani, MD	Associate Professor/ McGill University, Neurology and Neuroscience	Independent Clinical Expert

Precedent: SGC Open Chemical Probe Program



SGC Open Chemical Probe Program: Results To Date

Discovered

200+

Novel chemical probes developed in collaboration with industry and academic partners

Distributed

50,000+

Samples of chemical probes distributed globally by SGC and trusted vendors

Citations

13,000+

SGC chemical probes used by scientists around the world

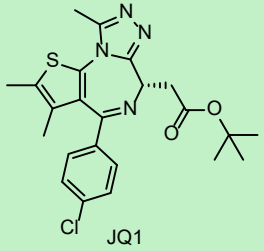
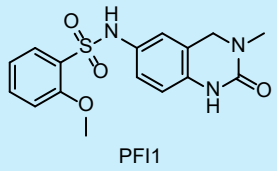
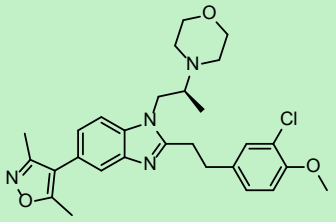
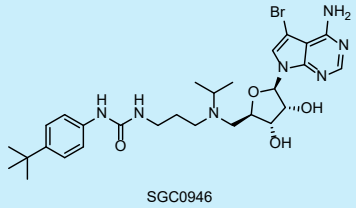
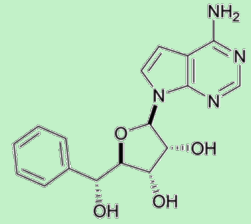
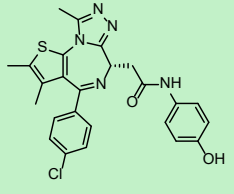
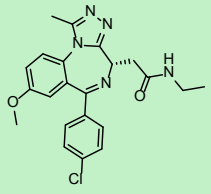
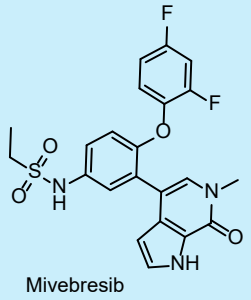
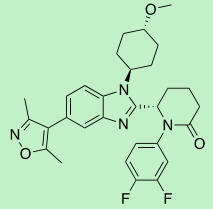
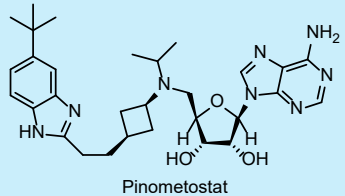
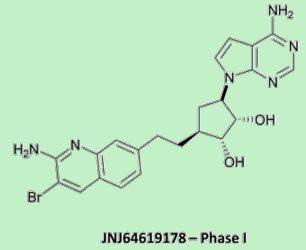
Clinical Trials

85+

Clinical trials and late-stage preclinical programs based on therapeutic hypotheses generated with SGC chemical probes

SGC Chemical Probes Seed Drug Discovery

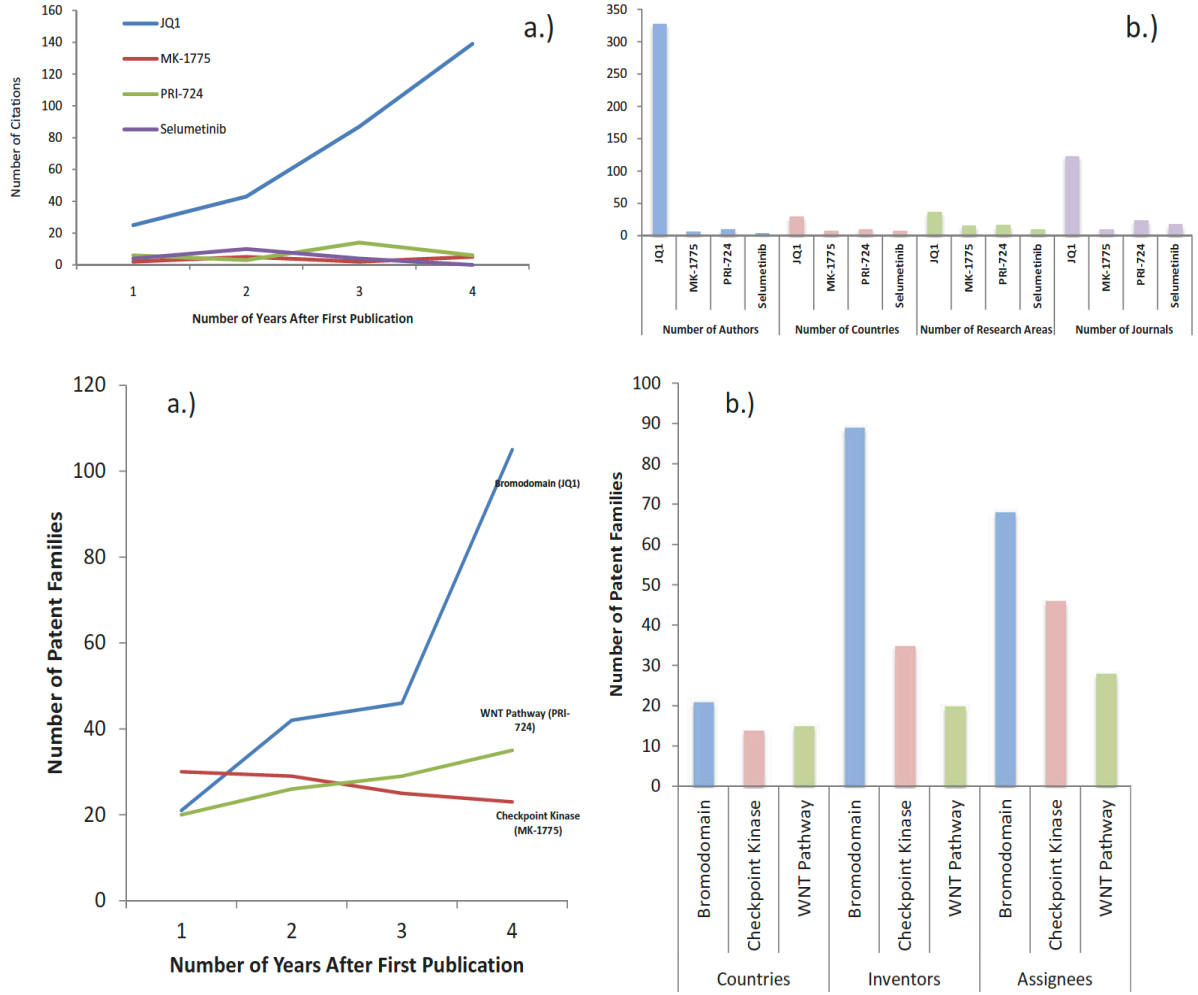
Examples of SGC Chemical Probe-Enabled Clinical Programs

	JQ1	PFI1	CBP-30	SGC0946	LLY-283
SGC Probe	 JQ1	 PFI1	 CBP-30	 SGC0946	
Clinical Candidate	 OTX105	 Molibresib	 Mivebresib		 Pinometostat	 JNJ64619178 – Phase I
	Phase 2b Solid Tumors MSD/ Mitsubishi Tanabe	**Phase 1** Advanced Lymphoma GSK	**Phase 1** Advanced Lymphoma GSK	**Phase 1/2** Prostate Cancer CellCentric	**Phase 1/2** Refractory Leukemia Epizyme/Celgene	**Phase 1** Advanced Lymphoma Solid Tumors Janssen

DOI: 10.1039/D1CB00016K

SGC Success Story: BET Inhibitors

- Epigenetic protein target: BRD4
  - Structure solved and deposited into PDB
- JQ1 chemical probe
  - Potent and selective chemical probe discovered and made publicly available through open SGC-GSK-Dana Farber collaboration
- Significant increases in downstream publication and patenting
  - Large number of companies, including SGC members, with downstream proprietary chemistry – 85 distinct patent families
- Several clinical programs ongoing
  - Various cancers
  - Dyslipidemia, CAD, diabetes



Source: Arshad et al. 2016

SGC Success Story: WDR5

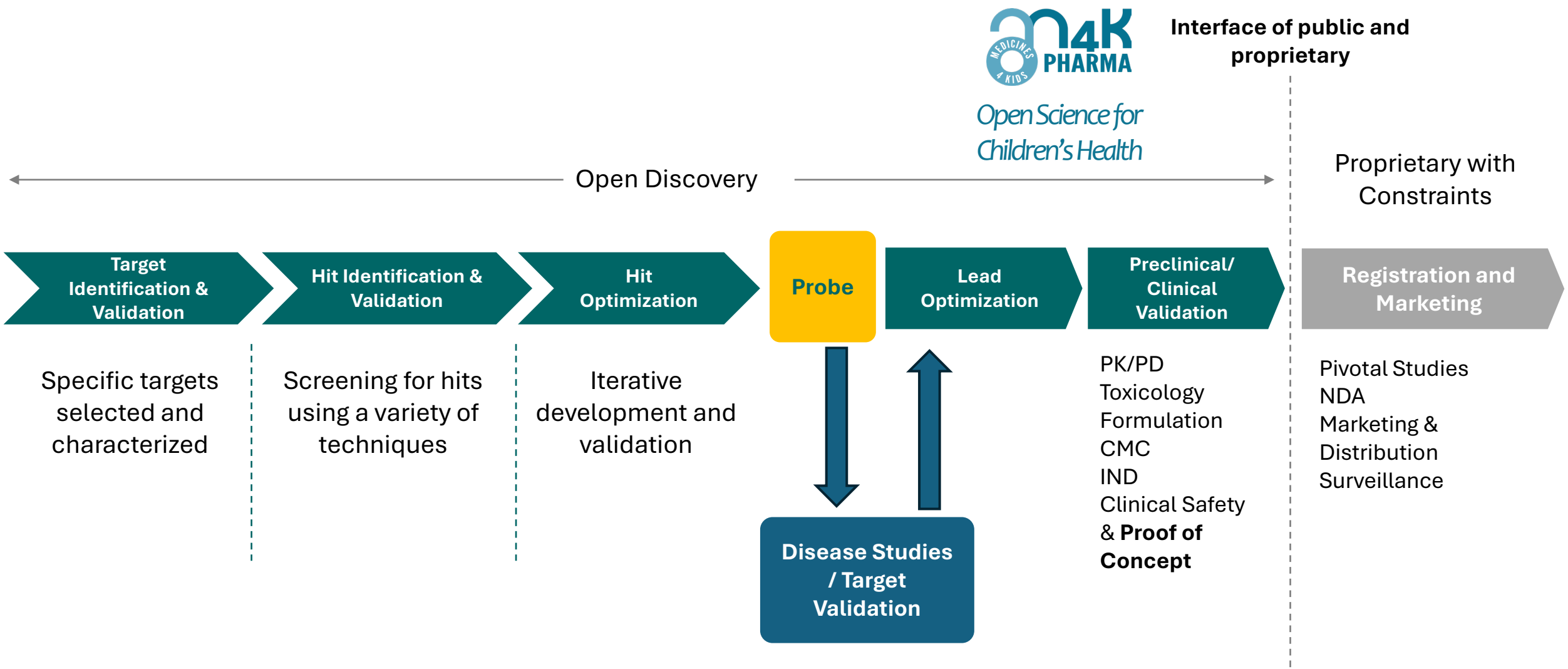
- Epigenetic protein target
  - Structure solved by SGC and openly deposited into PDB
- OICR-9429 chemical probe
  - Potent and selective chemical probe discovered and made publicly available through open SGC-OICR collaboration
- Disease linkage established by research community
  - WDR5 linked to various cancers (ALL, AML, solid tumours) using these public domain resources => therapeutic hypothesis and business case for investment
- Propellon Therapeutics
  - OICR team poised to act quickly re: expertise acquired through OS
  - Downstream proprietary chemistry spun-out from through FACIT
  - Celgene $1B+ deal announced Feb 2019

SGC

OICR
Ontario Institute for Cancer Research

FACIT
Fight Against Cancer Innovation Trust

M4K Pharma: Moving the SGC Open Chemistry Paradigm Downstream



SGC

M4K's DIPG Drug Development Pathway

Leverage non-dilutive capital and in-kind contributions via open science partnerships