Ovid® Therapeutics

GRAVITON BIOSCIENCE CORPORATION

Unlocking ROCK2 inhibition in the CNS

A COLLABORATION WITH GRAVITON BIOSCIENCE

April 2023

Disclaimers and forward-looking statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 including, without limitation, statements regarding the timing and development of Ovid's product candidate pipeline and achievement of expected near- and long-term milestones; the potential therapeutic benefits of Ovid's current or future product candidates and pipeline programs; the reporting of preclinical and clinical data for OV329 and GV101; the potential uses of OV329 and GV101; the clinical and regulatory development of OV329 and GV101; the likelihood that data for OV329 and GV101 will support future development and therapeutic potential; the potential development of GV101 and other ROCK2 inhibitor compounds in Graviton's library and the potential timing of GV101 clinical studies; the suitability of GV101 and Graviton's library of ROCK2 inhibitor compounds for a range of formulations and rare central nervous system administrations; the potential development of OV350 and other KCC2 compounds in the Company's library; the suitability of the Company's library of novel, direct KCC2 transporter activators for a range of formulations and administrations that would make it possible to pursue both chronic and acute epilepsies; the timing for filing of the Company's IND applications; the timing for the completion of Takeda's two pivotal Phase 3 trials evaluating soticlestat for Lennox-Gastaut and Dravet syndromes; the success of Takeda's trials in soticlestat; the success of any licensing or partnering opportunities, the success, timing, ability to attract and maintain strategic collaborations; the clinical and regulatory development and potential commercialization of soticlestat, OV329, GV101, OV350, or any of Ovid's other current or future product candidates and pipeline programs and market opportunities You can identify forward-looking statements because they contain words such as "will," "may," "plan", "believes", intends," "anticipates," "strives," "design," "advance," "target," "seek," "expects," and "potential" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances).

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GOAL

Change the world of orphan CNS therapy
with a novel mechanism of action: ROCK 2 inhibition,
and highly selective and safe compounds
that can act on endothelial and autoimmune
disorders of the brain
becoming staples in the treatment armamentarium

Collaborators to accelerate successful ROCK2i

- Pipeline of differentiated mechanisms for rare CNS & seizure-related disorders
- Repeat value creators via external innovation
- Veteran CNS development & commercial strategy team who supported launch or development of:
  - Ztalmy,®Fintepla,®Tysabri,® Gilenya,® Lecanemab,®Acthar Gel,® Brineura®

Ovid™ Therapeutics

- Pioneers of selective ROCK2 inhibitors
- Experts in RhoA/ROCK2 pathway
- Founders of KADMON, sold to Sanofi
- Successful developer of 1st next generation ROCK2 for GVHD
- Prolific drug discoverer/developers
  - Erbitux,® Rezurock®

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OVERVIEW

Collaboration attributes

Lead asset & portfolio of potentially highly selective ROCK2 inhibitors for rare CNS

- GV101 (Phase 1 completed in China; currently in pivotal formulation study in U.S.)
- Library of additional ROCK2 inhibitor compounds (~12)

GV101 has best-in-class potential

- Potentially more potent and more selective for ROCK2 than Rezurock,® REDX10843
- Well characterized safety profile (2 Phase 1 studies)
- Believed to be blood-brain barrier penetrant

Novel mechanism; rationale in multiple CNS indications

- ROCK2 is a signaling pathway that acts on actin cytoskeletal processes, cellular to extracellular matrix adhesion, fibrosis, autoimmunity
- Believed to be fit for CNS conditions with endothelial dysfunction & autoimmune MoAs

Regulatory precedent

- Prior ROCK2 approvals (Rezurock® in GVHD)
- Potential to leverage orphan and/or accelerated approval programs

Significant commercial opportunity

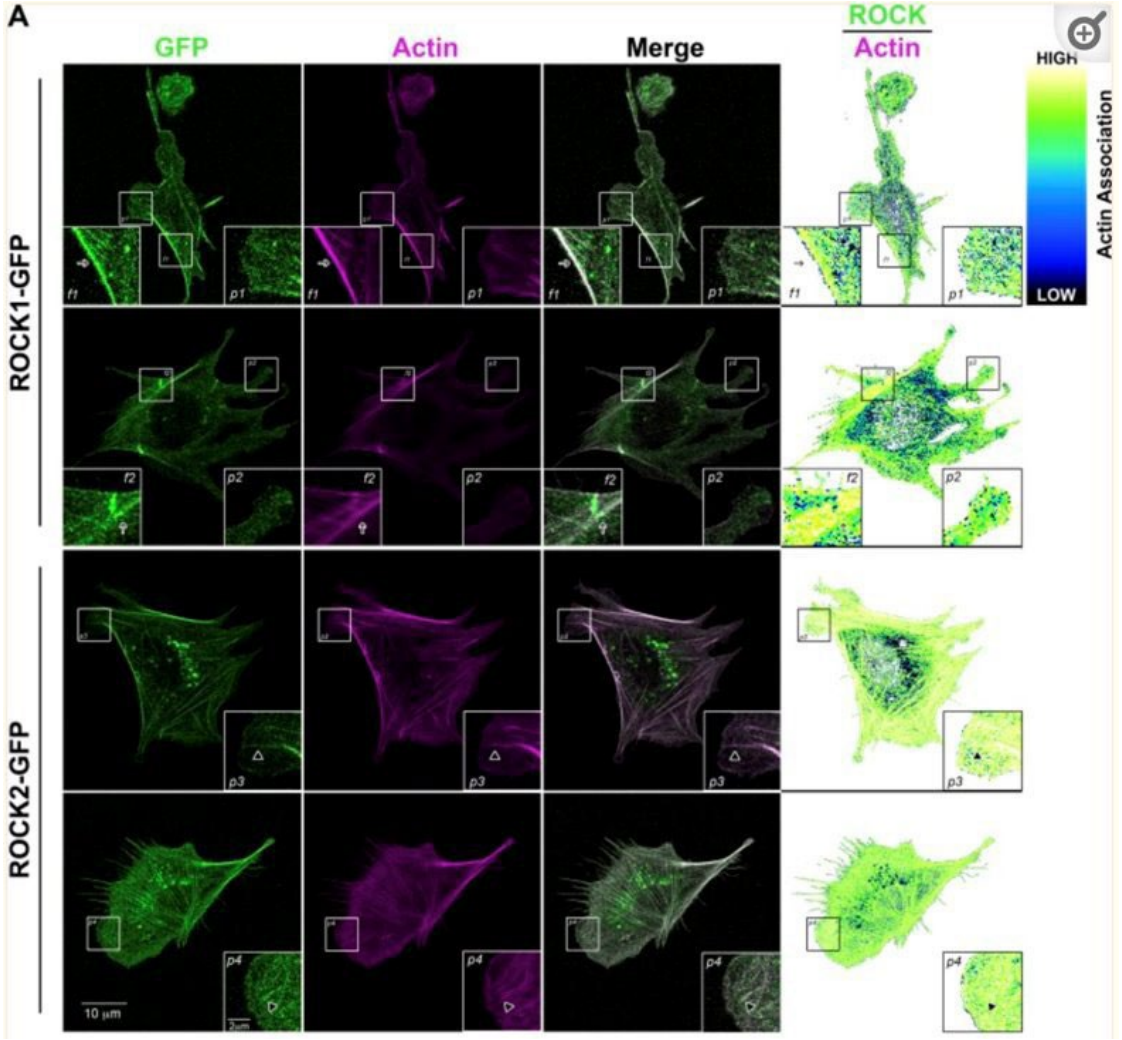
- Brainstem cavernous malformation is initial target orphan designation; then expand with potential for disease modification
- Expansive CNS utility

Transaction terms

Upfront investment	$10 million in the current preferred equity round of ~$50–$60M
Equity opportunity	Economic upside, outside the collaboration, in a broad range of ROCK2 inhibitor indications beyond CNS
Milestone payments	No milestone payments Royalties payable to Graviton under the agreement range from mid-to-high teens
Development & commercialization	Graviton conducts development through the end of Phase 2; under the License Agreement such development plans are to be mutually agreed on by the parties through the JDC Ovid will fund the development through agreed upon budgets and has decision-making authority Development and commercialization responsibility will transition over to Ovid post-Phase 2
Exclusivity to a library of compounds	Exclusive rare CNS rights to the lead asset (GV101) and ~12 other ROCK2i's optimized for CNS penetration & exposure

Why ROCK2 specific inhibition?

- ROCK1 and ROCK2 are highly homologous isoforms of the ROCK protein kinase that function differently
- ROCK inhibitors to-date have relatively equipotent inhibition against ROCK1 and ROCK2 isoforms
- Toxicity is associated with pan-ROCK inhibition, notably hypotension
- ROCK1 inhibition may counter therapeutic effects of ROCK2 inhibition
  - ROCK1 inhibition may potentially have different effects, such as abrogating the anti-pro-inflammatory effects of ROCK2
  - ROCK1 and ROCK2 have different effects on actin polymerization

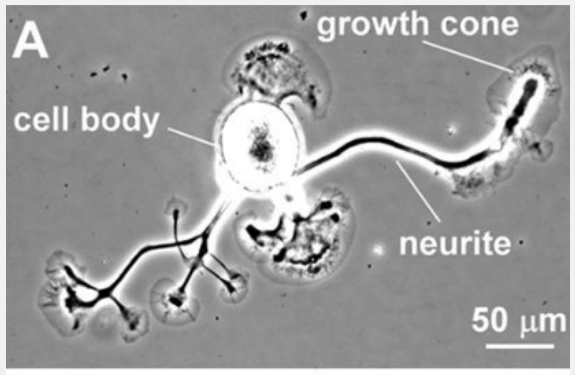


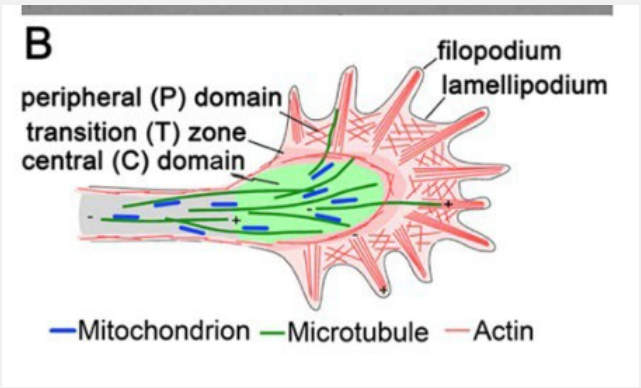
Newell-Litwa KA, Badoual M, Asmussen H, Patel H, Whitmore L, Horwitz AR. ROCK1 and 2 differentially regulate actomyosin organization to drive cell and synaptic polarity. *J Cell Biol.* 2015 Jul 20;210(2):225-42.

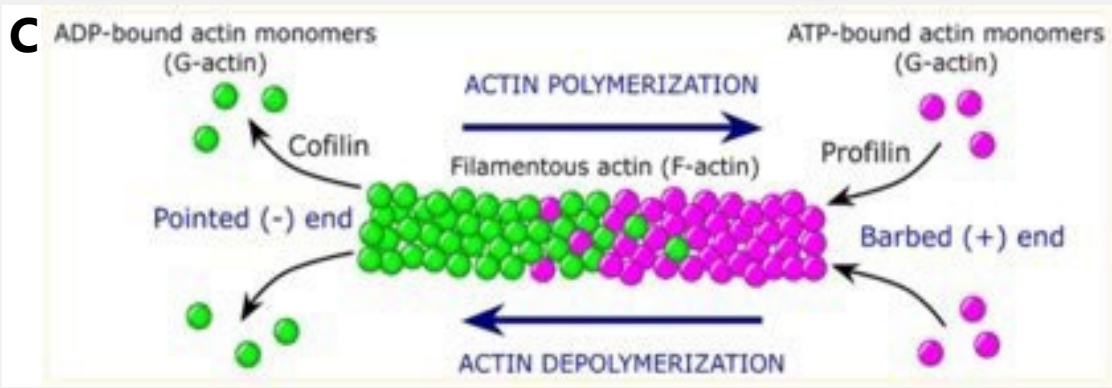
Therapeutic potential of ROCK2 inhibition: Endothelial disorders

In the CNS, ROCK2 inhibition can:

- Potentially promote growth and the cell-to-cell junction formation that is critical to endothelial function
- In neurons, is associated with increased neurite growth and decreased cell death







A – B. Miller KE, Suter DM. An Integrated Cytoskeletal Model of Neurite Outgrowth. Front Cell Neurosci. 2018 Nov 26;12:447. Adapted from O'Toole et al. (2015) with permission from Elsevier
C. Gibieža P, Petrikaitė V. The regulation of actin dynamics during cell division and malignancy. Am J Cancer Res. 2021 Sep 15;11(9):4050-4069.

Lead program: GV101

- Blood-brain barrier penetrant in animals
- Extensive preclinical safety & toxicology package
- Dosing completed for a Phase 1 SAD/MAD nano- suspension formulation (by TIDE Pharmaceutical)
- Plans to enter a gel cap formulation in a Phase 1, pbo-controlled randomized, double-blind, sequential MAD study in U.S.
- Modeled therapeutic plasma levels have been shown to be safe in animal models
- Cmax values up to 2 µ/ML

GV101's potential as a potent, selective, best-in-class ROCK2 inhibitor

	ROCK2 IC_{50} (uM)	ROCK1 IC_{50} (uM)	Selectivity (ROCK1/ROCK2)	BBB Penetrant	Off-Target Effects	Indication
GV101 Graviton BioScience Corp	**0.002-0.02**	**12.1**	**1071**	✓		**CCM**
REDX10843 RedX Pharma Plc	0.2	2.25	~100 fold	×		Fibrotic disease
KD025[1] Kadmon Pharmaceuticals	0.105	24	~80 - 100 fold	×		Graft vs host disease
NRL-1049[2] (Neurellis)	0.24 – 0.73	3.9 – 10.2	13.9 – 16 fold	✓	✓	CCM

Molecules with pan-ROCK inhibition have shown off-target effects

1 Ann Clin Transl Neurol. 2014 Jan; 1(1): 2–14. Published online 2013 Nov 19. doi: 10.1002/acn3.19

2 https://patents.google.com/patent/US10106525B2/en

Chart based on biochemical assays

Opportunity to leverage GV101 existing clinical program

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Single ascending dose in healthy adult volunteers in Q3, 2021

(nano-suspension)

- Conducted the first SAD with nanosuspension
- Q3 2021
- 2 cohorts, 8 ppl each (3:1)
- 400 mg and 800 mg
- 0 SAEs
- 1 headache, grade 1 400 mg group
- AUC approached limit 14,400 ng/mL and study was stopped

TIDE 泰德制药 TIDE PHARMACEUTICAL

Single & multiple ascending dose in healthy adult volunteers Q2-Q4, 2022

(nano-suspension)

- Double-blinded, placebo controlled,
- 50 male/female healthy adult volunteers
- Nanosuspension formulation with 7-day consecutive dosing:
  - SAD: 400 mg, 800 mg, and 1200 mg
  - MAD: 200 mg and 400 mg
- Endpoints: Safety & tolerability; PK
- 0 SAEs
- AE of interest (headache (21%), diarrhea (11%), nausea/vomiting (2%)
- Similar AUC to U.S. study (AUC 11,600 in 1,200 mg group)

UPCOMING

Multiple ascending dose est. initiation Q3, 2023

(gel cap)

- Randomized, placebo-controlled, double-blind, single-center MAD, FE and cQT
- 8 per dose group
- 3:1 randomization
- 7-day dosing, 72-hour trailing PK data collection

Phase 1: Tide MAD nanosuspension

Nanosuspension MAD study at 200 mg and 400 mg

T_{max} 3.5-4 hours
$T_{1/2}$ 12-14 hours
Steady state at 96 hours

Linear PK
2-3x accumulation

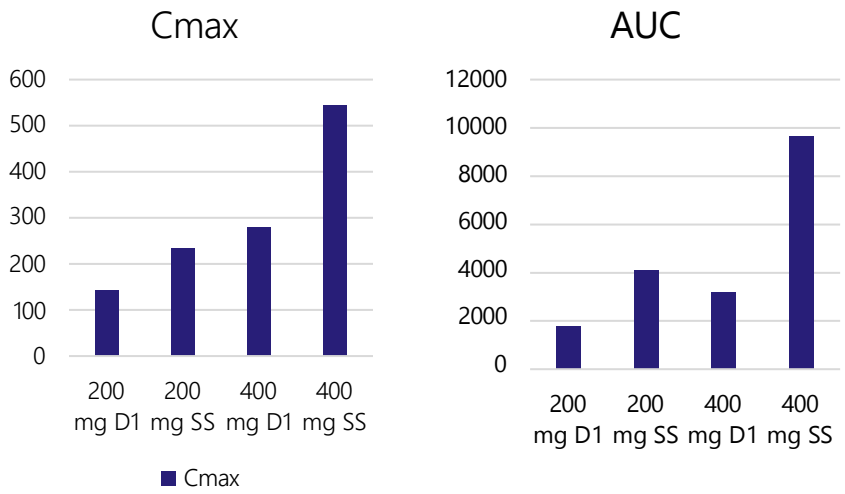


Table of AEs, Tide MAD

200 mg	AE	Treated	Placebo	400 mg	AE	Treated	Placebo
Clinical	Headache	1|1		**Clinical**	Headache	12|2	
	Knee pain	1|1			Diarrhea	2|2	
Labs	ALT increased	1|1	1|1		Nausea	1|1	
	Amylase increase	1|1		**Cardiac**	T wave abn		2|1
	Bilirubin increase	1|1		**Vitals**	Heart rate increase	2|1	
	CPK increase	1|1			Hypertension	1|1	
	Glucose increase	1|1		**Labs**	ALT increase	1|1	
	RBC/Hct decrease	2|2			AST increase	1|1	
	WBC decrease*	1|1			Bilirubin increase*	4|3	
	WBC increase	1|1			CPK increase**	2I2	
					GGT increase	2|1	
					Hg Decrease	1|1	2|1

*Grade 2 **Grade 1 or 4
23 of 28 AEs in treated ppl were in 2 ppl

POTENTIAL 1ST INDICATION: **Brainstem cavernous malformations**

- Mechanistic rationale for reversing hyperactivity of ROCK; restoring barrier function of endothelial cells
- Early animal model POC
- Unmet need
- Rare disease with no pharmacologic therapy
- Potential to gain proof of concept with smaller subset prior to a larger registrational trial
- Measurable endpoints (radiographic)
- Possibility of accelerated path to market

Brainstem cavernous malformations

Presentation & prevalence

- Mulberry-shaped abnormal blood vessels with thin, leaky walls located in the brain and or spinal cord, which increase over age
- 2nd most common intracranial vascular malformation in humans
- Present in ~0.5% of the population (~1.6M in U.S.)[1]
  - ~20% of which have brainstem involvement[2]

CCMs located in the brainstem pose unique challenges

- Brainstem CCMs are a key risk factor for brain bleeds, can cause significant morbidity due to repeated hemorrhaging
- 82% of patients with brainstem lesions involve major fiber tracts, making surgery extremely difficult[2]
- Guidelines indicate that surgical resection of brainstem CCM could be considered only after a second symptomatic bleed given risks associated with the surgery
  - Post operative mortality and morbidity are high among patients who undergo surgery to remove brainstem lesions
  - 53% of the cases experience post operative neurologic deficits[2]

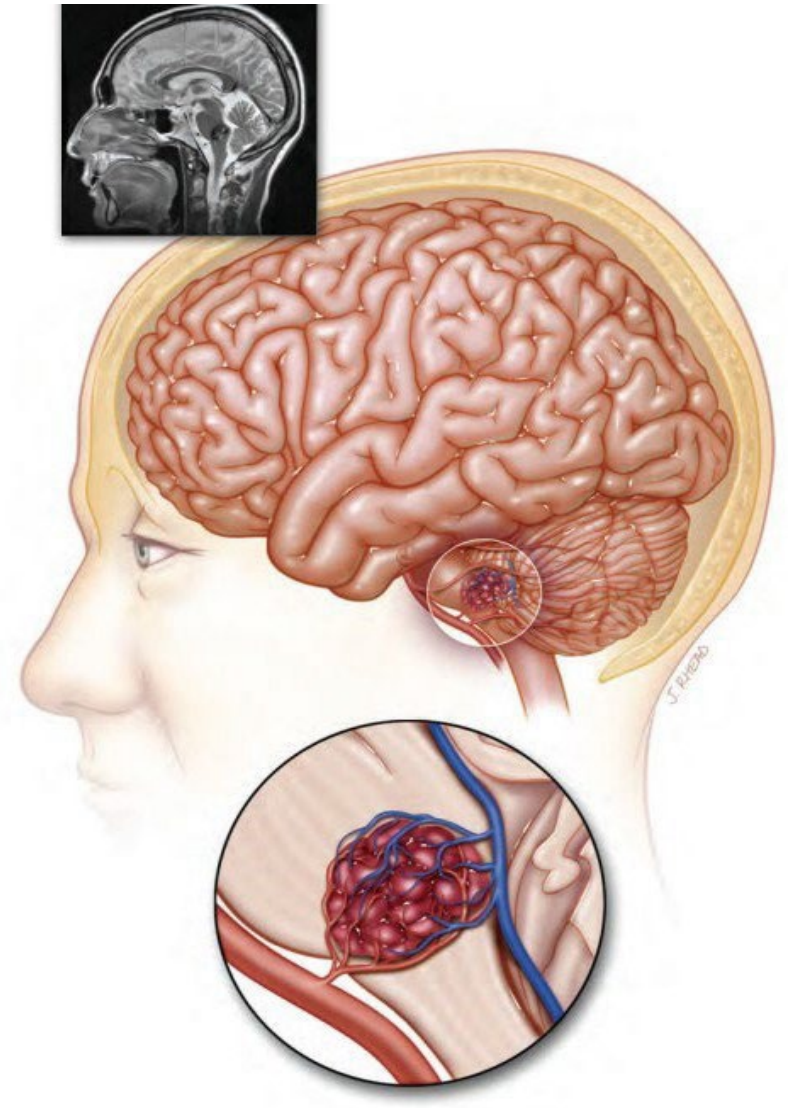


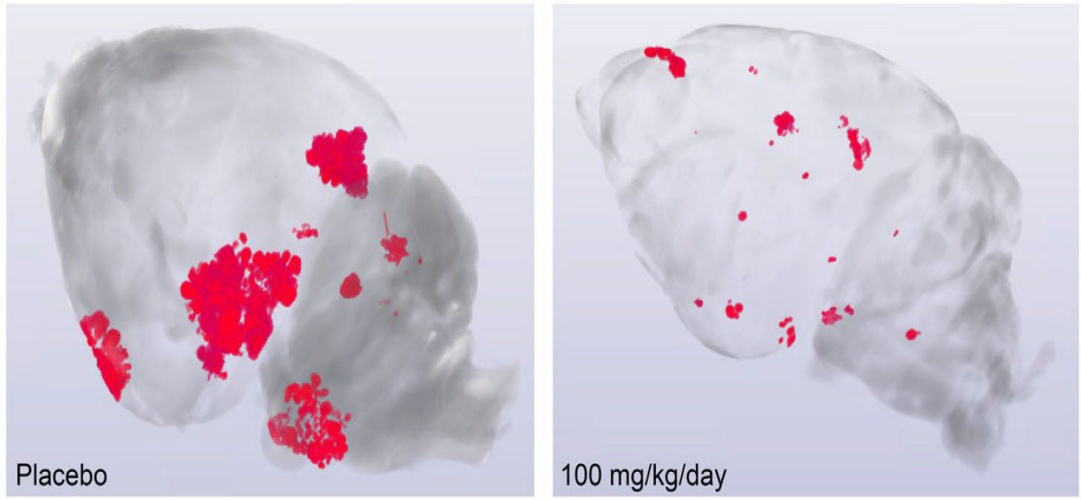
Image attribution: Brainstem angioma from Alliance to Cure Cavernous Malformation

1. Flemming KD, Graff-Radford J, Aakre J, et al. Population-Based Prevalence of Cerebral Cavernous Malformations in Older Adults: Mayo Clinic Study of Aging. JAMA Neurol. 2017;74(7):801–805. doi:10.1001/jamaneurol.2017.0439
2. Caton MT, Shenoy VS. Cerebral Cavernous Malformations. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538144/

Mechanistic rationale for brainstem cavernous malformations

- ROCK is hyperactive in brain capillary endothelial cells in patients with CCM
- A potent, selective ROCK2 inhibitor seeks to repair the endothelial cell defect to reduce the permeability of the blood–brain barrier
- Preclinical studies have shown that ROCK2 inhibitors:
  - Reduce lesion size and genesis
  - Restore the barrier function of endothelial cells
  - Reverse hyperactivation of ROCK
- In CCM transgenic mice, ROCK2 inhibitors reduce the leakiness of lesions, prevents the growth and formation of lesions, and slows disease progression

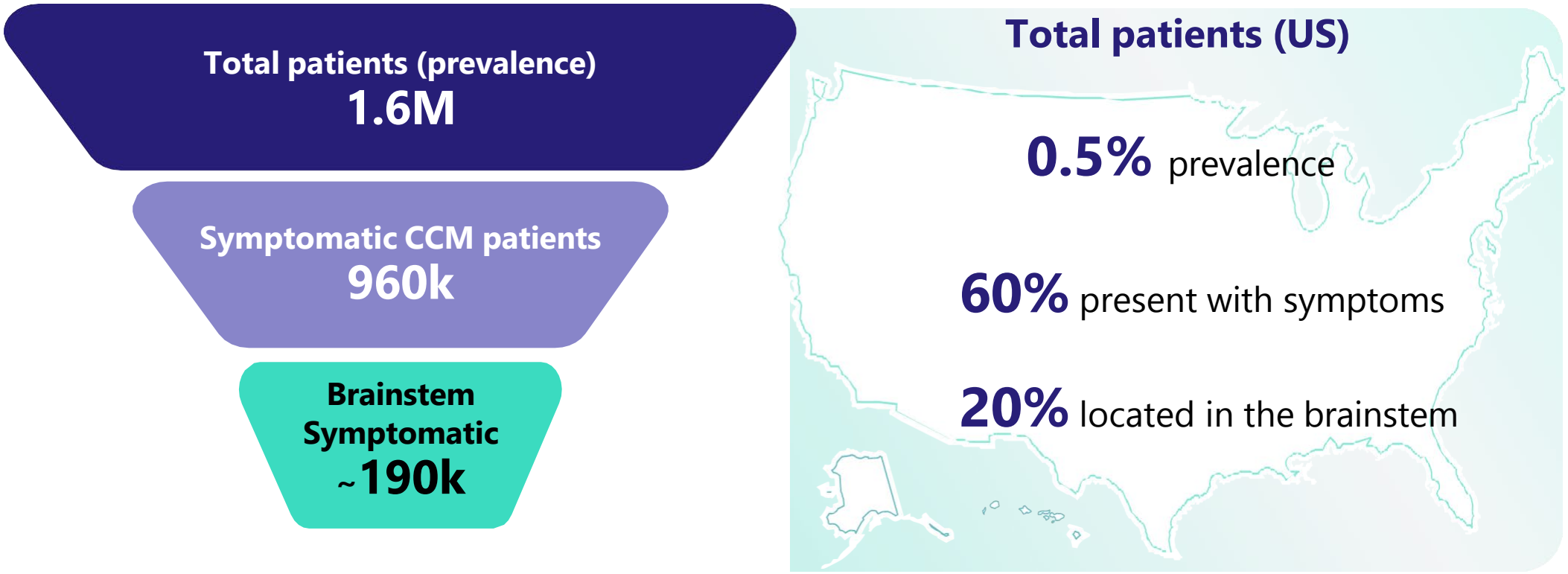
ROCK2 inhibition appeared to reduce the lesion volume and lesion sites



*Micro-CT imaging of the brain of ccm1$^{+/-}$ mice
Dosed with: ROCK2 inhibitor BA-1049

SOURCE: McKerracher L.; et. al. Translational Stroke Research (2020) 11:365-376

Significant opportunity
Brainstem CCM ~190,000 individuals in U.S.



Note: does not include discounts, access cut, compliance cut

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6924279/pdf/nihms-1059977.pdf
https://www.ncbi.nlm.nih.gov/books/NBK1293/
Otten P, Pizzolato GP, Rilliet B, Berney J. [131 cases of cavernous angioma (cavernomas) of the CNS, discovered by retrospective analysis of 24,535 autopsies]. Neurochirurgie. 1989;35(2):82-3, 128-31.

ROCK2 inhibitor development strategy

1. **Demonstrate CNS penetration and characterize safety**
2. **MAD study to confirm pivotal formulation (100 mg/200 mg)**
3. **Proof-of-concept demonstration in high-need subset: brain stem hemangiomas**
   - Target: Patients with cavernous angioma in the brainstem
   - Possible endpoints: Lesion size reduction, lesion bleed reduction (MRI); rate of symptomatic bleed, change in size of hemispheric and cerebral angiomas
4. **Pivotal study (Brainstem or familial cavernous malformations)**
   - Possible endpoints: Primary = Lesion size reduction (MRI); Secondary = Avoidance of surgery, effect on rebleed

Graviton collaboration advances Ovid strategy

Rare CNS & seizure-related disorders

- Initial indication: Cerebral cavernous malformations (CCM)
  - 50% of patients have seizures
- ROCK2i validated MoA in CCM animal models

Differentiated, multi-MOA pipeline

- Potential novel, selective ROCK2 inhibitor
- GV101 in Phase 1; library of ROCK2i compounds
- Potentially BBB penetrant; small molecule
- Complementary to other mechanisms

Broad therapeutic potential

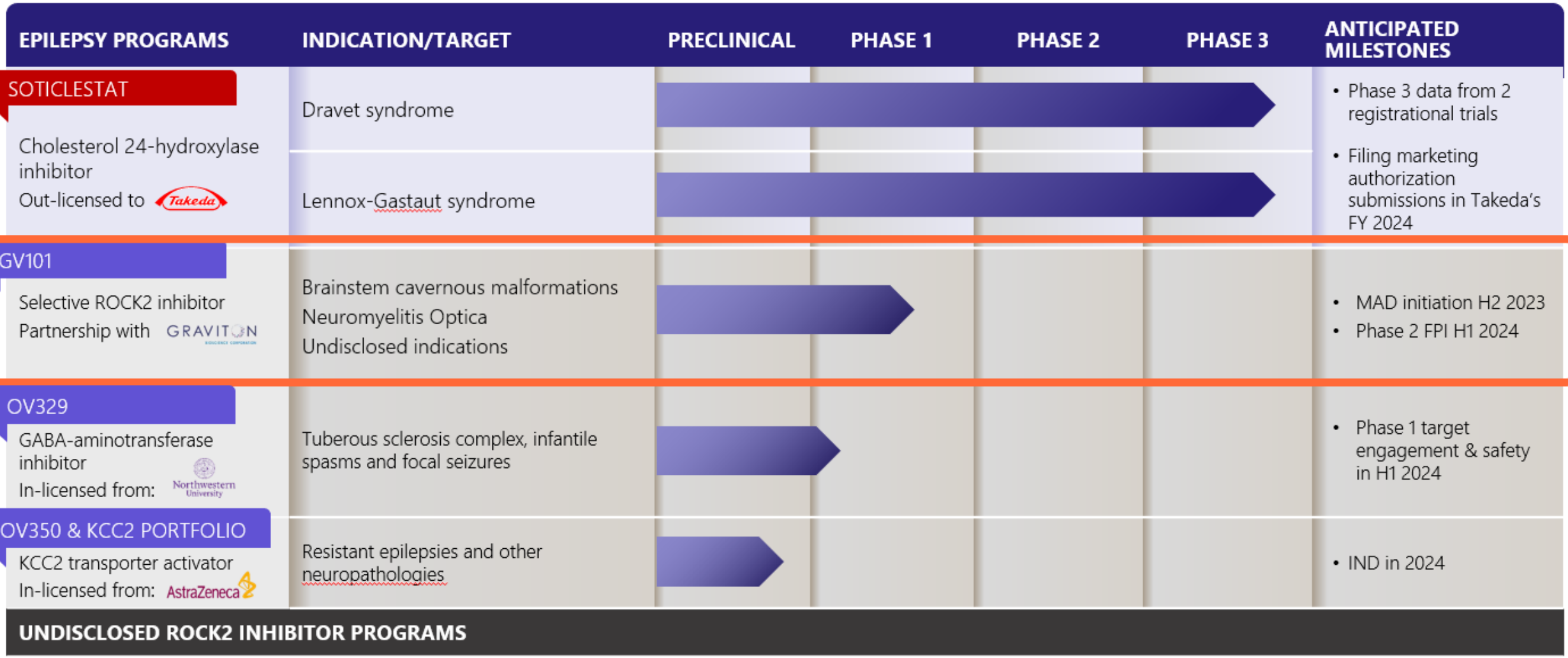
Potential to explore in CNS:

- Endothelial dysfunction and autoimmune disorders, including:
  - Myelin associated disorders
  - Tauopathies
  - TBI and brain injuries

Multiple near-term milestones

- Pivotal formulation YE 2023
- Potential Phase 2 POC 2025
- IND for additional indications

Adds clinical-stage asset to Ovid epilepsy & seizure franchise



Future leaders in ROCK2i for the brain

- Potential best-in-class, ROCK2 inhibitor with franchise of follow-on assets
- Opportunity for rapid POC trial in brainstem malformations
- Regulatory precedent for class
- Significant potential commercial opportunity
- Potential broad therapeutic applicability of ROCK2 inhibition in CNS

Ovid® Therapeutics

Conquering epilepsies & brain disorders with courageous science