Funding should never be the reason a promising hemangioblastoma therapy doesn’t get tested.

Research grants for hemangioblastomas of the brain and spine in von Hippel-Lindau disease. Real money behind the first experiments, answers in 60 days, and capital that stands behind what works.

$3 million

committed over three years. Applications open January 2027.

$100k–$500k

Breakthrough Grants, five to ten times a typical VHL grant. No equity, no IP claim.

60 days

to a decision, with a reason. Rolling applications, no deadlines.

WHAT WE FUND

Therapies that could be used alongside belzutifan[1] or in place of it, with better long-term tolerability, for hemangioblastomas of the brain and spine. We also fund the models, delivery methods and markers that make those therapies possible.

HOW TO APPLY

Fill in the one-page application online. It takes about fifteen minutes. For every eligible proposal, the funding team seeks advisory opinions from clinicians with no involvement in that proposal. The final decision rests with the pool’s directors, who give every applicant an answer and a reason within 60 days.

WHO IS ELIGIBLE

Any compound or approach is eligible if you can show, with evidence and references, that it reaches hemangioblastomas of the brain or spine at a therapeutic level, or set out a credible path to getting it there.

Work that started in renal cell carcinoma is welcome on those terms.

Where this started. The pool is inspired by a donation already in process from the Rath Family Foundation to the Hemangioblastoma Lab at Massachusetts General Hospital, and is built so more funders, labs and families can do the same thing at the same rung.

WHAT WE ASK

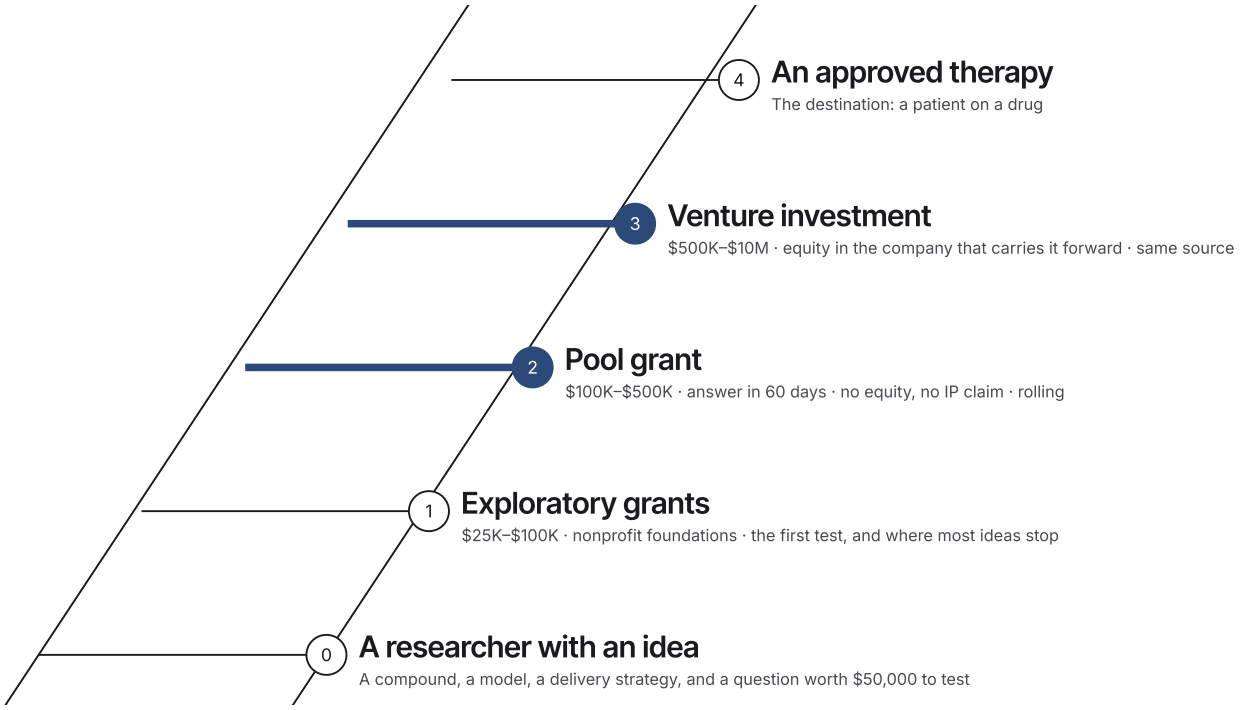
Quarterly updates, data shared with the field, milestones agreed up front. Every grant, result and cost is published so the next condition starts with a map.

BEYOND THE GRANT

When funded work is ready to become a company, the same source follows with $500,000 to $10 million of venture investment as equity. Returns, if any, seed the next pool.

Money moves a project up each rung.

> **Most ideas for rare conditions stop after a first exploratory grant. The step after it, $100,000 to $500,000 to turn a result into a program, has no natural funder: NIH takes a year to answer and rarely funds it, and investors want a company first. The pool pays for that rung, and the one above it.**



WHERE THE WIDER PIPELINE BREAKS

Every rare condition crosses the same eight stages. Three have no natural funder (shaded amber). The pool covers the two before the clinic; the venture tier reaches the next two.

Diagnosis	Gene and mechanism	**Readiness assets**	**IND-enabling and CMC**	**Phase 1/2**	**Pivotal and FDA**	**Make and launch**	Access and follow-up

Of roughly 10,000 rare conditions, 392 have ever had an approved therapy, and 85–89% have never had a sponsor file an orphan designation.[2] Rare programs that reach the clinic are approved at twice the rate of common-disease programs.[3] What kills them is never starting.

Built to be copied. The structure is the same for the next condition: name the stage where it is stuck, fund that stage to the hand-off, stand behind what works, and publish what it cost.

We have made extraordinary progress on kidney cancer. Yet brain and spine hemangioblastomas, and the fear of deficits from multiple procedures, have always been at the forefront for VHL patients.

Hemangioblastoma treatments are currently the greatest unmet medical need in VHL. But this condition gets a small fraction of the research time and funding. We are establishing this hemangioblastoma pool to fix that problem.

16
FDA-approved systemic agents for renal cell carcinoma, across 24 approved regimens, since 1992[4]

1
FDA-approved systemic therapy for CNS hemangioblastoma — belzutifan, 2021, on 24 evaluable patients[1,5]

66%
of deaths in a contemporary 336-patient VHL cohort were caused by CNS hemangioblastoma[6]

0
minimally invasive options for hemangioblastomas of the brain or spine

WHERE THE RESEARCH ACTUALLY GOES

MEASURE	KIDNEY	HEMANGIOBLASTOMA	RATIO
Interventional drug trials ever registered	1,654	10	**165 : 1**
All interventional trials ever registered	2,218	13	**171 : 1**
Published clinical trials (PubMed, publication type)	2,257	25	**90 : 1**
Publications, all time	56,077	2,878	**19 : 1**
Publications, 2024–2026	9,197	310	**30 : 1**
NIH funding, FY2024–25 combined	$151.0M	$1.4M	**107 : 1**
NIH projects ever titled “hemangioblastoma”	33–34 / yr	0	—
Industry trials ever listing it as a condition	—	1	—

Publication and trial counts are reproducible queries run 12 October 2026 against PubMed and the ClinicalTrials.gov API;[7] funding from NIH RePORTER abstract-field search.[8] The single industry trial is a Novartis phase 2 of vatalanib that enrolled eleven patients and began in 2003.[9] There has not been another in twenty-three years, and there is no active industry trial in this compartment anywhere today.

The publication gap is widening, not closing. All-time 19:1, last decade 27:1, last three years 30:1. And the trial gap is five to six times worse than the publication gap — hemangioblastoma is described about twenty times less often than kidney cancer, but trialed about ninety times less often.

THE RATE-LIMITING STEP

Half of these tumors never grow, 72% of those that do grow in bursts, and only 6.3% ever become symptomatic — which is why the definitive natural-history study, 1,921 lesions over 15,819 lesion-years, concludes that “unpredictable growth of hemangioblastomas compromises assessment of nonsurgical therapies.”[10] Measuring benefit is the gate every drug in this compartment has to pass through, and it is still shut. Solving it is pre-competitive, unglamorous, and exactly what industry will not pay for — which is what makes it the right first use of philanthropic money rather than a complaint about the field.

WHAT CHANGED, AND WHAT DID NOT

In 1990, the natural history of VHL was described in 152 patients. Median actuarial survival was 49 years, and the paper's closing sentence named "renal cell carcinoma the leading cause of death."[11] That was the correct diagnosis of the problem, and the field acted on it.

Over the thirty-four years since, the kidney compartment received sixteen approved drugs across twenty-four regimens, nephron-sparing surgery, percutaneous cryoablation and thermal ablation, a validated intervention threshold, and transplantation as a backstop.[4] Two more regimens arrived in 2026 alone — in one year, the kidney gained twice as many approved regimens as the brain and spine have in all of history.

The 3 cm rule deserves specific credit. In 181 VHL patients followed a mean of 58 months, not one of the 108 whose largest renal tumor stayed under 3 cm developed a metastasis; above 3 cm, 27% did.[12] That single threshold converted renal VHL into a surveillance problem with a planned, repeatable intervention at a known trigger — and the organ tolerates it. In one series, fifty patients underwent seventy-one operations with a mean of 14.7 tumors removed per kidney, and none required renal replacement therapy.[13] It is one of the most effective guidelines in any hereditary cancer syndrome, and for most people with VHL it holds.

It worked. In the contemporary cohort, renal cell carcinoma is no longer a statistically significant predictor of overall survival (HR 1.55, 95% CI 0.75–3.23, p=0.24).[6] That is one of the quiet successes of modern medicine, and the people in this room built it.

Hemangioblastoma of the brain and spine received, in the same thirty-four years, one drug. It is now the leading cause of death in this disease, and an independent predictor of mortality where renal cell carcinoma is not. There is no 3 cm rule for the brain — no threshold, no repeatable intervention, and no backstop if the organ fails.

> "The main cause of death is still CNS hemangioblastomas and hence improved treatment options are essential."
>
> Binderup et al., J Med Genet 2017 — the Danish national cohort: every known VHL family in Denmark, genotype-confirmed, with a non-VHL sibling control arm.[14]

THE ATTRIBUTION HAS REVERSED

CAUSE OF DEATH — CONTEMPORARY COHORT, N=336, 12,966 PERSON-YEARS	DEATHS	SHARE	INDEPENDENT PREDICTOR OF SURVIVAL
CNS hemangioblastoma	45	66.2%	**Yes — HR 2.43, p=0.001**
Renal cell carcinoma	20	29.4%	No — HR 1.55, p=0.24

Zhou et al., Front Oncol 2019.[6] Pancreatic neuroendocrine tumor (HR 0.53, p=0.14) and pheochromocytoma (HR 0.81, p=0.73) were also not independent predictors; retinal hemangioblastoma was (HR 2.44, p=0.004). Follow-up ran from birth with organ involvement as a time-dependent covariate, avoiding immortal-time bias. CNS disease also presents earlier — median onset 30 years, against 36.5 for the kidney. 3 cm data: Duffey, J Urol 2004.[12] Nephron-sparing series: Herring, J Urol 2001.[13]

AND THE AUTHORS NAME THE COROLLARY THEMSELVES

> "Such discrepancy can partially [be] explained by… targeted therapy, minimally invasive surgery and active surveillance for RCCs… On the other hand, the pharmacological and surgical treatment for CHB are required to be further improved."
>
> Zhou et al., 2019[6] — the shift is attributed by the authors to investment in the kidney, and they name the corollary themselves.

WHAT THESE PATIENTS ACTUALLY CARRY

Surgeons in this room will say, correctly, that a hemangioblastoma operation is usually survived with function preserved, and the published rates support them. Most deterioration recorded at discharge resolves by three to six months,[15,16] and in the largest prospective VHL cohort — 225 patients over a mean 6.9 years — only 4% sustained a lasting drop in performance status attributed to operative morbidity.[10]

That is not where the burden is. The burden is what accumulates across a lifetime of them.

In the Japanese national registry of 168 operated spinal hemangioblastomas — 101 sporadic, 67 VHL, mean follow-up 53.6 months — sporadic patients improved significantly between discharge and six months. The VHL patients did not improve at all, and then tended to decline. At final follow-up, 22.4% of the VHL patients required assistance to walk or used a wheelchair, against 4.0% of the sporadic patients. The reason sits in the same table: 70.1% of the VHL patients had already had brain tumor surgery, against 1.0% of the sporadic group.[17]

> "In VHL disease, short-term functional prognosis is expected to be adequate if there is no history of CNS tumor surgery, but thereafter the risk of functional deterioration increases with each surgery because of the tendency for new lesions to appear in the CNS."
>
> Takeshima et al., Neurospine 2023 — Neurospinal Society of Japan, 58 centers, nationwide.[17]

PERMANENT DISABILITY BY ORGAN, IN THE SAME 128 PATIENTS

FUNCTION PERMANENTLY IMPAIRED	PATIENTS	MEAN AGE AT SURGERY, THAT ORGAN
Central nervous system — sensory or motor	34 (26.5%)	27.8 years
Vision	21 (16.4%)	—
Hearing	16 (12.5%)	—
Kidney — requiring dialysis	2 (1.5%)	36.5 years

Feletti et al., Neuro Oncol 2016[18] — 128 VHL patients followed prospectively from 1996. The authors could find no existing measure of disability in VHL and had to construct one. In the same patients, permanent CNS disability runs seventeen times permanent renal disability. One was left in a vegetative state after cerebellar surgery. The CNS figure does not separate disability caused by the tumor from disability caused by its treatment — and no study has ever separated them.

The deficits that remain are also the ones the field measures least. At follow-up in a five-center European spinal series, residual sensory deficit was present in 60.8%, gait disturbance in 37.3% and motor deficit in 25.5% — while the median McCormick grade, the standard outcome measure for these operations, was unchanged.[19] After upper-cervical myelotomy, permanent sensory and gait dysfunction reached 43% with the McCormick grade again showing no significant change.[20] The scale the field grades this surgery on is not sensitive to what patients actually lose: numbness, position sense, balance, continence, and pain that outlasts the operation by years.

The patient-reported data, such as it is, shows a dose–response. Across 220 people with VHL in five countries, EQ-5D health state fell from 0.825 in those who had never had surgery, to 0.803 after one, to 0.705 after two or more. Among those who could recall their most recent operation, 51.8% said it worsened their fatigue, 51.2% their mental health, and 45.2% their ability to go about daily life.[21] That survey was funded by the manufacturer of the one approved drug, and its instruments are not validated in VHL; we cite it because it is the only data of its kind that exists in this disease.

Nobody has ever measured the cumulative deficit burden across a VHL patient's lifetime of CNS operations. That absence is itself the argument.

FREQUENTLY ASKED QUESTIONS

Why not fund kidney work that will also help the brain?
Because the thing that has repeatedly failed to transfer is precisely the brain. Sunitinib: 33% response in renal lesions, 0 of 21 in hemangioblastoma.[22] Pazopanib: 52% renal, 2 of 49 hemangioblastoma.[23] Sunitinib again, in VHL patients: 64% renal response, every CNS lesion stable.[24] Three cohorts, three drugs, one direction. The dissociation is the best-replicated fact in VHL therapeutics, and it is the reason a kidney-first strategy has not reached the brain.

Is this a general VHL project?
No. It funds hemangioblastoma of the brain and spine. VHL is the reason those tumors occur, not the scope of the project. Proposals in renal cell carcinoma, pancreatic neuroendocrine tumor, pheochromocytoma or endolymphatic sac tumor are out of scope even when the applicant is a VHL researcher.

Then why does the overview say work from renal cell carcinoma is welcome?
Because most of the mechanistic groundwork in this disease was done in kidney cells, and we would rather import it than wait. The condition is strict: show, with evidence, that the compound reaches a hemangioblastoma of the brain or spine at a therapeutic level, or set out a credible path to getting it there. A kidney-derived hypothesis is eligible. A kidney endpoint is not.

Why not retinal hemangioblastoma?
Because the approved drug already works there. In the ocular subgroup of its pivotal trial, all sixteen eyes with evaluable active retinal lesions were graded improved — 100% at a median thirty-seven months, with no new lesions and no ocular progression.[25] That is the result we want in the brain and do not have. Retinal disease is not finished business, but it is the one hemangioblastoma compartment where the existing drug performs as well as anyone could ask of it. The brain and spine are where it does not.

Isn’t belzutifan already the answer?
Partly, and more than most people realize — in the solid component of CNS lesions the response rate is 76%, which is better than its own renal response rate.[5] But it is one drug, taken indefinitely, with anemia in roughly nine patients in ten, and in its own pivotal trial at fifty months the commonest reason for stopping it was the patient’s own decision to withdraw.[26] One drug is not a therapeutic area.

FREQUENTLY ASKED QUESTIONS, CONTINUED

Isn't the real problem surgical, not pharmacological?
Surgery here is excellent and still not enough. In the most experienced center in the world, 98% of operations improved or stabilized symptoms and there were no radiographic recurrences — and the same 80 patients still required 126 craniotomies for cerebellar lesions alone.[16] The result is good; it just has to be done again, and again, and the patient does not come all the way back each time. See *What these patients actually carry*, earlier. A drug that keeps one operation from being necessary is worth more here than in any compartment where the operation is repeatable at low cost.

Why can't you ablate these the way you ablate a renal lesion?
Anatomy, not technique. A hemangioblastoma is a highly vascular tumor embedded in non-regenerating eloquent tissue inside a closed bony compartment. There is no survivable thermal margin, no equivalent of losing some nephrons, and no equivalent of dialysis or transplant if the organ fails. In one series, ten patients received thirty-two separate renal ablation sessions treating fifty-seven tumors, with a mean eGFR loss of 5.5 mL/min over seven and a half years.[27] There is no CNS analogue to that at any price.

Is this just a bigger grant?
It is a specific missing rung. Exploratory grants of $25–100K exist, and venture capital exists once there is a company. The step between — $100–500K to turn a result into a program — has no natural funder. NIH takes a year and rarely funds it; investors want a company first. We pay for that rung, answer in sixty days with a reason, and take no equity and no IP. We also pay for the rung above it, which is the next question.

What is the honest reason this gap exists?
Market size, and it is nobody's fault. Roughly 688,000 Americans are living with kidney cancer;[28] roughly 3,700 have VHL-associated CNS hemangioblastoma.[29] That is 187 to 1, and trial activity sits almost exactly on it. No company is behaving badly. But public funders sit at 107:1 and 104:1 — at parity with the commercial incentive rather than correcting for it — and philanthropy has no such excuse either. That is the whole argument for this project.

What would $3 million actually change?
Total identifiable public funding for hemangioblastoma research is about $2.4 million.[8] A commitment the size of a single kidney-cancer R01 would more than double the world's funded research in this compartment. There is no crowded field to enter here. There is, as yet, barely a field.

What happens if a grant actually works?
There is capital waiting above it, and that is the part of this structure worth understanding. A grant of $100–500K is sized to produce a decisive result, not a product. If that result begins to look like a therapy, a further $3–10 million of venture funding is available behind it — separate from the $3 million grant pool, and enough to reach the two things this field cannot currently afford: a single-cell atlas run alongside an arrayed drug screen, which we price at $2.7–4.1 million,[30] and the preclinical development behind a first therapeutic candidate. The grant itself stays non-dilutive — no equity, no IP. The tier above it is venture capital on venture terms. What disappears is the gap between the two, and that gap is where a promising hemangioblastoma result currently dies: too far along for a pilot grant, too early for an investor who wants a company first.

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30. Authors' costing; not drawn from a published source. The $2.4 million public-funding figure is from NIH RePORTER (reference for NIH funding above).