

## Category

Best Startup

## General Information

### Company Name \*

SEED Therapeutics

### Turnover and/or Funding

Company Information

Company Name: SEED Therapeutics

Number of Employees: 11-50

Turnover and/or Funding: \$53 million raised through investment, upfronts, and milestones

Sub-Category: Biotechnology

Corporate Name: SEED Therapeutics, Inc.

Therapeutic Areas: Oncology, Neurodegeneration, Immunology, and Virology

### Overview

SEED Therapeutics is a clinical-stage biotechnology company focused on developing molecular glues against undruggable targets to improve human health. Molecular glues harness the power of the ubiquitin-proteasome system (UPS) for target protein degradation (TPD) found in all cells. SEED's co-founders include TPD Nobel Prize laureate Dr. Avram Hershko, HHMI Investigator and University of Washington Professor Ning Zheng who coined the phrase "Molecular Glue" for TPD, HHMI Investigator and NYU School of Medicine Chair of Department of Biochemistry and Pharmacology Professor Michele Pagano who is an expert in UPS and cell biology, and Dr. Lan Huang, CEO of SEED and SEED's parent NASDAQ company BeyondSpring, and a pioneer in defining UPS protein structures.

SEED has been recognized as a global leader in the TPD field in two 2024 "Nature" review articles. Its proprietary RITE3™ platform was developed to overcome the challenges in molecular glue discovery. It uses novel E3 ligases (E3) to detect unfolded or mutant proteins with no druggable pockets, the 80% of disease-causing proteins not targetable with traditional methods. RITE3™ is a multidimensional platform including structural, biochemical and cell-based methods to select the E3, from over 600 E3s in the human genome comprised of two structural classes of HECT and RING Domain E3s, as the right one to target proteins for degradation. SEED has developed a robust pipeline with 9 programs using 6 Novel E3s in multiple indications, including Oncology, Neurodegeneration, Immunology, and Virology. SEED's technology is further validated with investment and R&D partnerships from global pharma, including Eli Lilly and Eisai.

### Current Impact:

While many TPD companies are applying established technologies and developing PROTACs (considered TPD1.0) with two well-characterized E3s, Cereblon- or VHL-based, a Nature Biotechnology Review (2024) acknowledged SEED's TPD2.0 approach, "SEED Therapeutics is amongst those who are nevertheless working to let other E3 ligases shine".

SEED's lead asset, ST-01156, a first-in-class, novel brain-penetrant degrader of RBM39, an RNA splicing factor overexpressed in multiple hard-to-treat cancers, affecting over 1 million cancer patients globally. The initial indication, Ewing sarcoma, is a rare and aggressive pediatric tumor with no new approved therapies in over 30 years. ST-01156 demonstrated total tumor regression in Ewing sarcoma models, which could be due to its precise target engagement to degrade RBM39, thereby eliminating EWS-FLI1 fusion protein, a driver gene fusion causing 90% of Ewing Sarcoma cases. An IND for ST-01156 was filed in July 2025 and is advancing into the clinic with leading U.S. institutions. As stated in Nature Reviews Drug Discovery 2024, "Armed with a better understanding of RBM39 biology, SEED is set to advance an optimized RBM39 degrader into the clinic next year."

SEED is developing an oral Tau degrader for Alzheimer's and related neurodegenerative diseases, which could reach over 50 million patients worldwide.

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### **Sub-Category \***

Biotechnology

### **Background**

**Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions)  
(please be as specific as possible in your description; limit 500 words)**

World-class Founders, Management Team and Board

SEED Therapeutics is built on a foundation of deep scientific vision and collaborative execution. SEED was founded in Nov. 2020 by four of the most influential scientists in TPD:

Dr. Avram Hershko, 2004 Nobel Laureate in Chemistry - discovered the UPS over 50 years ago;

Dr. Ning Zheng, HHMI Investigator at the University of Washington - solved the first RING domain E3 ligase (2002) and coined the term "molecular glue" (2007);

Dr. Michele Pagano, HHMI Investigator and Chair of Biochemistry Department at NYU Medical School - defined key SCF ubiquitin ligase mechanisms and ubiquitin biology (since 1995);

Dr. Lan Huang, Chairman, CEO - solved the first HECT E3 ligase structure (1999) and integrates structural insight with therapeutic development; a serial biotech entrepreneur for over 15 years.

The scientific team has a combined track record of 40 INDs and 12 NDAs.

Dr. James Tonra, President and CSO - held leadership positions at ImClone and Regeneron and helped bring 5 novel oncology drugs to approval.

Dr. Bill Desmarais, CFO and CBO - brings decades of experience in biotech/pharma strategy and deal-making.

Dr. Eric Rowinsky, Senior Clinical Advisor; led the development of Erbitux and over 10 first-in-class targeted oncology drugs to approval.

SEED's Board of Directors includes independent members, Mr. Tai and Mr. Tung, members from Lilly and Eisai, and Dr. Huang and Dr. Tonra from management.

Jackson Tai, former JP Morgan banker and CEO of DBS Bank. Served on boards of Eli Lilly, Mastercard, and HSBC,

Ko-Yung Tung, former General Counsel of the World Bank, former senior partner at O'Melveny & Myers, and retired director of Eisai.

Dr. Linus Lin (Director from Lilly), Managing Director of Lilly Chorus. Previously General Manager of Lilly China Research.

Dr. Yoshiharu Mizui, (Director from Eisai), President of Eisai Innovation, Inc.

#### Validation by Global Pharma

SEED has been supported by leading global pharma, including Eli Lilly and Eisai as investors and R&D collaborators. SEED raised \$40M plus \$13M in upfront payments and early milestones. Between the two R&D collaborations, there is the potential to earn > \$2.3B in milestones and royalties.

#### Impact on Human Health

SEED's unique TPD platform has the potential to target 80% of the disease-causing proteins that are currently undruggable. SEED has developed a robust pipeline with 9 programs in multiple indications, including Oncology, Neurodegeneration, Immunology, and Virology, including a lead oncology asset, a first-in-class RBM39 degrader, with the potential of targeting over 1 million cancer patients globally in mechanism-targeted indications and an oral Tau degrader for Alzheimer disease, which could reach over 50 million patients worldwide.

Our founders are active architects of scientific strategy, anchoring SEED in the most rigorous domains of structural biology and therapeutic design. The executive and clinical teams translate that science into operational excellence, and board members contribute with the judgment and perspective of seasoned global leaders. This leadership model gives SEED the clarity, resilience, and credibility to pursue one of medicine's most difficult frontiers.

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#### **History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations) \***

**(please be as specific as possible in your description; 500 words)**

Lead Drug Candidate: ST-01156

ST-01156 is an orally administered, brain-penetrating, selective, small molecule degrader of RBM39. RBM39 is an RNA splicing protein upregulated in multiple tumor types. Despite previous efforts, past compounds had issues with oral delivery, safety, and patient selection. ST-01156 has notable antitumor activity in nonclinical studies with total tumor regression in a number of mechanism-targeted cancers. It has a favorable safety profile, which supports clinical development for several tumors.

#### Intellectual Property

SEED filed a composition of matter, provisional patent in May 2023, and a PCT in 2024. If granted, the composition will be protected until May 2044.

#### Mechanism of Action

ST-01156 enables binding of DCAF15 E3 ligase and RBM39, causing the ubiquitination of RBM39 and its degradation by the proteasome. Recent preclinical data suggest several cancers could respond to an RBM39 degrader.

#### Preclinical Experience

ST-01156 demonstrated superb anticancer activity with total tumor regression in several animal models. A favorable safety profile was observed, with low potential for adverse off-target effects. In immunocompromised mice bearing Ewing sarcoma xenografts, oral administration of ST 01156 resulted in complete tumor regression. Treatment of Ewing sarcoma cells with ST 01156 induced complete RBM39 degradation, accompanied by elimination of pathogenic EWS-FLI1 fusion transcript and reduction in proteins involved in DNA-damage repair.

Complete tumor regression was observed in models of neuroblastoma and colon cancer.

Brain penetration was shown in animal models with RBM39 degradation in the neurons.

ST-01156 exhibited low potential for cardiovascular effects at pharmacologically active exposures, with minimal hERG inhibition (IC50 >50 µM).

Safety pharmacology endpoints in 4-week GLP toxicology studies revealed no drug-related effects on CNS function, FOB assessments, respiratory parameters, or cardiovascular assessments in rats or dogs. Pharmacodynamic (PD) studies using PBMC in multiple species demonstrated target engagement-RBM39 degradation soon after treatment with ST-01156. These support using RBM39 levels in PBMCs as a PD biomarker for faster selection of optimum clinical dose.

## Clinical Plan

SEED's development plan includes a sequence of clinical trials and regulatory submissions to expand from Ewing sarcoma into broader RBM39-dependent malignancies.

ST-01156's initial target is Ewing sarcoma, a rare and aggressive pediatric tumor for which no new therapies have been approved in over 30 years. Ewing sarcoma affects approximately 200 children and adolescents annually in the U.S., with a five-year survival rate under 20% for relapsed cases. Treatment requires intense chemotherapy and radiation with long-term side effects. In 2025, the U.S. FDA granted ST-01156 both orphan drug and pediatric disease designations for Ewing sarcoma.

ST-01156 may represent the first targeted therapy for this disease by degrading RBM39 and eliminating EWS-FLI1, the oncogenic fusion protein that drives 90% Ewing Sarcoma tumor biology. SEED's approach is tissue-specific, and biomarker-enabled.

ST-01156 attracted clinical investigators from leading U.S. institutions: Drs. George Demetri (Dana Farber), Bob Maki (Memorial Sloan Kettering), and Gordi Rodon (MD Anderson), are fully embedded in our clinical operations. Each of them is actively involved in trial planning, patient selection, and disease expansion strategy. Their experience spans early-phase clinical trials, sarcoma translational science, academic-industry collaboration, and drug approval.

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## **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition \***

### The Problem

Proteins are essential to body function, but when mutated or misfolded, they can cause disease. About 80% of these disease-related proteins lack druggable sites and are untreatable with current methods. Nature targets these aberrant proteins via the TPD system. One prominent example is the naturally derived molecular glue, Revlimid. Revlimid binds the E3 ligase, Cereblon, triggering degradation of the transcription factor, Ikaros, helping to treat multiple myeloma. It achieved annual peak sales of \$12.8 B before it was discovered as a molecular glue, underscoring the enormous patient reach of molecular glue drug candidates.

The biotech industry has worked hard to discover novel degraders for disease proteins. TPD1.0 was a PROTAC approach with large bi-functional molecules (M.W. > 800 Dalton) linking known E3s: Cereblon or VHL to disease proteins. PROTACs are limited due to their large size and potential for off-target toxicity as well as the Hook-effect. TPD2.0 consists of molecular glues, smaller molecules that have better drug-like features (M.W. < 500 Dalton). These can link both E3s and disease proteins together without requiring pockets on either protein.

## The Solution

Historically, molecular glues, such as Revlimid, have been discovered serendipitously. SEED replaces that randomness with structural, computational, and biochemical precision. The key to de novo design is in finding the "right E3 ligase" among over 600 human E3s.

Our TPD platform is designed for "right E3" discovery and translation. Each candidate is evaluated for potency, selectivity and a match between target expression, disease tissue, and degradative mechanism, producing a robust, rational foundation for both pipeline expansion and regulatory confidence.

## Lead Oncology Asset: First-in-class RBM39 Degradar ST-01156

ST-01156 represents a new modality for one of the most aggressive pediatric cancers, Ewing Sarcoma, and it has the potential to be a broad anti-tumor agent. Using our deep understanding of E3 DCAF15 structure and ubiquitin biology, rational mechanism-based cancer indication selection, and artificial intelligence-assisted physiologically based modeling, SEED aims to achieve meaningful and potent efficacy with a clear therapeutic window in targeted cancers.

Aryl sulfonamides were developed as cytotoxic anti-cancer agents before they were discovered as RBM39 degraders. They failed to maintain low RBM39 levels with intravenous dosing, limiting their anti-cancer efficacy. Previous RBM39 degraders, including E7820, have other drawbacks such as low anti-cancer potency and hERG inhibition.

ST-01156 demonstrated improved anticancer activity, metabolic stability, and oral bioavailability compared to E7820. Unlike E7820, ST-01156 did not inhibit hERG suggesting it has a more favorable safety profile.

Several preclinical hematological and tumor models support the use of RBM39 degraders as monotherapy. There is ample preclinical support for combination strategies with inhibitors of poly (ADP-ribose) polymerase, and cyclin-dependent kinase 4/6.

ST-01156 demonstrated total tumor regression in several mechanism-targeted models, including Ewing sarcoma, neuroblastoma, and colon cancer. It showed potent anti-cancer activity against several patient-derived models, including carcinoma of the liver, biliary duct, testes, and uterus/endometrium.

SEED's RITE3™ platform represents a fundamental change: moving from empirical discovery to rational, structure-guided engineering of molecular glue degraders, with potential to improve human health in millions of patients.

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**Please provide appropriate references (PubMed, Abstract, Website) \***

References

Website: [www.seedtherapeutics.com](http://www.seedtherapeutics.com)

TPD Pioneering Discoveries from SEED Co-Founders

- Hershko A. et al. Proposed role of ATP in protein breakdown: Conjugation of proteins with multiple chains of the polypeptide of ATP-dependent proteolysis. *Proc. Natl. Acad. Sci. USA.* 77(4): 1783-1786 (1980).
- Pagano M. et al. Role of the Ubiquitin-Proteasome Pathway in Regulating Abundance of the Cyclin-Dependent Kinase Inhibitor p27. *Science* 269(5224):682-5 (1995).
- Huang L et al. Structure of an E6AP-UbcH7 complex: insights into ubiquitination by the E2-E3 enzyme cascade. *Science* 286(5443):1321-6 (1999).
- Zheng N et al. Structure of the Cul1-Rbx1-Skp1-F boxSkp2 SCF ubiquitin ligase complex. *Nature* 416: 703-709 (2002).
- Tan X. et al. Mechanism of auxin perception by the TIR1 ubiquitin ligase. *Nature* 446(7136):640-5 (2007) - Coined "molecular glue", from Prof. Zheng lab
- Cao S et al. Defining molecular glues with a dual-nanobody cannabidiol sensor. *Nature Communication* 13: 815 (2022) - Features of Nature's "molecular glues" to increase binding between E3 and protein of interest, from Prof. Zheng lab
- SEED's Unique TPD Platform featured in "Nature" Review
- Garber K. The glue degraders. *Nature Biotechnology* 42(4):546-550 (2024).
- Mullard A. Protein degraders push into novel target space. *Nature Review Drug Discovery* 23(11):799-802 (2024)
- TPD with Potential to Target >80% Disease Protein Currently Undruggable
- Taavi K. Neklesa, James D. Winkler, Craig M. Crews. Targeted protein degradation by PROTACs, *Pharmacology & Therapeutics*, 174:138-144 (2017)
- RBM39 Science
- SEED AACR 2025 Presentation: Liu F. et al. Targeting Ewing Sarcoma with A Novel RBM39 Degrader: DNA Damage Repair Pathway Effects (Abstract 1556)
- Shulman DS, Merriam P, Choy E, Guenther LM, Cavanaugh KL, Kao PC, Posner A, Bhushan K, Fairchild G, Barker E, Klega K, Stegmaier K, Crompton BD, London WB, DuBois SC. Phase 2 trial of palbociclib and ganitumab in patients with relapsed Ewing sarcoma. *Cancer Med.* 12(14):15207-15216 (2023) - This combination showed objective response (ORR) at 0%, underscoring severe unmet medical needs in relapsed Ewing Sarcoma.
- Xu C, Chen X, Zhang X, Zhao D, Dou Z, Xie X, Li H, Yang H, Li Q, Zhang H, et al. RNA-binding protein 39: a promising therapeutic target for cancer. *Cell Death Discov.* 7:214 (2021).
- Han T, Goralski M, Gaskill N, Capota E, Kim J, Ting TC, Xie Y, Williams NS, Nijhawan D. Anticancer sulfonamides target splicing by inducing RBM39 degradation via recruitment to DCAF15. *Science.* 356(6336): 3755 (2017)
- Talbot DC, von Pawel J, Cattell E, Yule SM, Johnston C, Zandvliet AS, Huitema AD, Norbury CJ, Ellis P, Bosquee L, et al. A randomized phase II pharmacokinetic and pharmacodynamic study of indisulam as second-line therapy in patients with advanced non-small cell lung cancer. *Clin Cancer Res.* 13:1816-1822 (2007).
- Assi R, Kantarjian HM, Kadia TM, Pemmaraju N, Jabbour E, Jain N, Daver N, Estrov Z, Uehara T, Owa T, et al. Final results of a phase 2, open-label study of indisulam, idarubicin, and cytarabine in patients with relapsed or refractory acute myeloid leukemia and high-risk myelodysplastic syndrome. *Cancer* 124:2758-2765 (2018).
- Mita M, Kelly KR, Mita A, Ricart AD, Romero O, Tolcher A, Hook L, Okereke C, Krivelevich I, Rossignol DP, et al. Phase I study of E7820, an oral inhibitor of integrin alpha-2 expression with antiangiogenic properties, in patients with advanced malignancies. *Clin Cancer Res.* 17:193-200 (2011).
- Haddad RI, Weinstein LJ, Wiczorek TJ, Bhattacharya N, Raftopoulos H, Oster MW, Zhang X, Latham VM, Jr., Costello R, Faucher J, et al. A phase II clinical and pharmacodynamic study of E7070 in patients with metastatic, recurrent, or refractory squamous cell carcinoma of the head and neck: modulation of retinoblastoma protein phosphorylation by a novel chloroindolyl sulfonamide cell cycle inhibitor. *Clin Cancer Res.* 10:4680-4687 (2004).

- Mossmann D, Muller C, Park S, Ryback B, Colombi M, Ritter N, Weissenberger D, Dazert E, Coto-Llerena M, Nuciforo S, et al. Arginine reprograms metabolism in liver cancer via RBM39. *Cell*. 186:5068-5083 (2023).
- Bewersdorf JP, Stahl M, Taylor J, Mi X, Chandhok NS, Watts J, Derkach A, Wysocki M, Lu SX, Bourcier J, et al. E7820, an anti-cancer sulfonamide, degrades RBM39 in patients with splicing factor mutant myeloid malignancies: a phase II clinical trial. *Leukemia*. 37:2512-2516 (2023).
- Nijhuis A, Sikka A, Yogev O, Herendi L, Balcells C, Ma Y, Poon E, Eckold C, Valbuena GN, Xu Y, et al. Indisulam targets RNA splicing and metabolism to serve as a therapeutic strategy for high-risk neuroblastoma. *Nat Commun*. 13:1380 (2022).
- Xia A, Yue Q, Zhu M, Xu J, Liu S, Wu Y, Wang Z, Xu Z, An H, Wang Q, et al. The cancer-testis lncRNA LINC01977 promotes HCC progression by interacting with RBM39 to prevent Notch2 ubiquitination. *Cell Death Discov*. 9:169 (2023).
- Kohsaka S, Yagishita S, Shirai Y, Matsuno Y, Ueno T, Kojima S, Ikeuchi H, Ikegami M, Kitada R, Yoshioka KI, et al. A molecular glue RBM39-degrader induces synthetic lethality in cancer cells with homologous recombination repair deficiency. *NPJ Precis Oncol*. 8:117 (2024).
- Chen WC, To MD, Westcott PMK, Delrosario R, Kim IJ, Philips M, Tran Q, Bollam SR, Goodarzi H, Bayani N, et al. Targeting KRAS4A splicing through the RBM39/DCAF15 pathway inhibits cancer stem cells. *Nat Commun*. 12:4288 (2021).
- Pogacar Z, Johnson JL, Krenning L, De Conti G, Jochems F, Liefink C, Velds A, Wardak L, Groot K, Schepers A, et al. Indisulam synergizes with palbociclib to induce senescence through inhibition of CDK2 kinase activity. *PLoS One*. 17:e0273182 (2022).

\*Kindly clearly label your files with company name and asset name.

Attached Files:

- [SEED Therapeutics ST01156.docx](#)