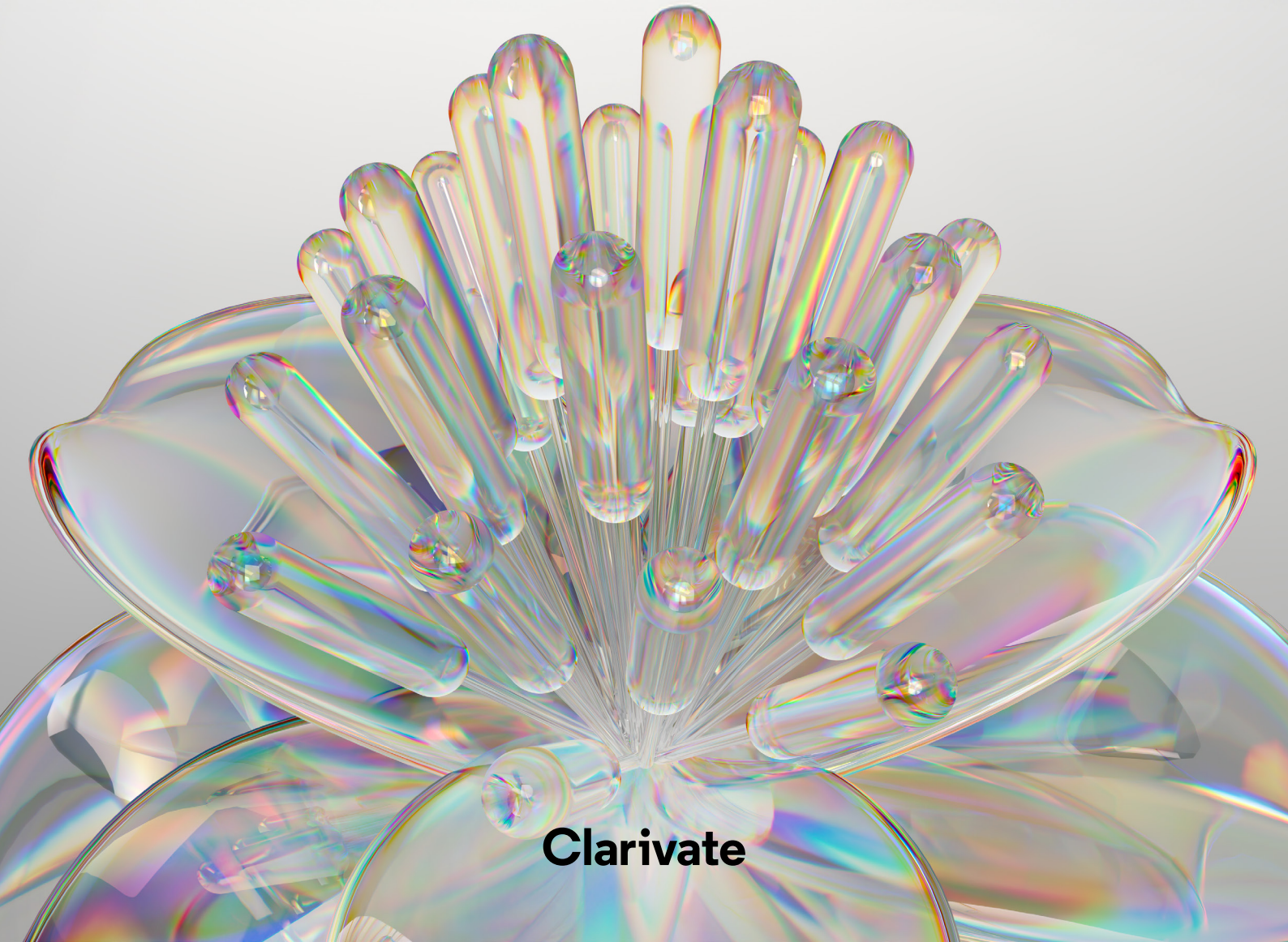
Protein degraders enabling precision interventions for 'undruggable' targets

Companies to Watch 2025



Clarivate

6 innovators changing the drug discovery and development paradigm

A look at emerging standouts in the field of protein degrader therapeutics, including:

Potential benefits of their products for patients and caregivers

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Financing, patent filings and R&D activity to date

What sets them apart from the pack and makes them Companies to Watch

Contents

Methodology

To select our Protein Degrader Companies to Watch, we weighted companies according to factors including:

- Medical, business and scientific challenges these companies are attempting to solve;
- Whether the company has demonstrated proof of concept and achieved key developmental milestones;
- Positioning in clinical trials;
- Relationships with notable scientific and academic institutions;
- Patient unmet need and/ or burden of disease their solutions aim to address;
- Financial positioning, including funding secured, relationships with industry and institutional investors, financial runway and prospects for future fundraising or partnerships; and
- Ownership and status of intellectual property (IP) estate.

Clarivate analysts assessed the changing protein degrader landscape with a variety of proprietary data sources:

BioWorld is the industry's leading suite of news services delivering actionable intelligence and the most innovative therapeutics and medical technologies in development.

Cortellis Clinical Trials Intelligence is a comprehensive source of detailed insights on clinical sites and trial protocols including biomarkers, targets and indications.

Cortellis Competitive Intelligence provides access to data such as drug pipeline, deals, patents, global conferences and company content, along with the latest industry news and press releases. The Cortellis Competitive Intelligence Drug Timelines & Success Rates methodology is a patented analytic tool that applies statistical modeling and machine learning to more reliably and accurately forecast drug development milestones, timelines and probability of success. The AI-enhanced search in Cortellis Competitive Intelligence provides an intuitive way to search using natural language questions.

Cortellis Deals Intelligence ccombines the industry's largest source of deals intelligence with enhanced visualizations of the highest quality data, to quickly find the optimal deal without compromising due diligence. Cortellis Deals Intelligence combines a robust and comprehensive source of deals intelligence predictive analytics dashboard uses data science techniques, including a combination of automated machine learning and human intelligence, to accurately predict deal valuation and probability of success for partnered assets.

Cortellis Drug Discovery Intelligence is a trusted source of biological, chemical, pharmacological and patent data in a single platform.

OFF-X preclinical and clinical safety intelligence is a unique translational tool providing drug and class safety intelligence to anticipate risks and drive new competitive value.

These and other Clarivate data sources provide high-quality, curated data for our proprietary AI capabilities that form the mainstay of our intelligence solutions and services, including advanced search algorithms, bespoke consulting and predictive analytics (e.g., Drug Timelines and Success Rates).

In order to ensure that our information was up to date and accurate, we reached out to the companies our analysts identified as potential Companies to Watch. The companies featured in this report responded, while other companies who did not respond are not included in the report. This varied response rate resulted in a list skewed toward Western-based countries, not reflecting the rapid pace of innovation in Mainland China and elsewhere in the Asia-Pacific region.

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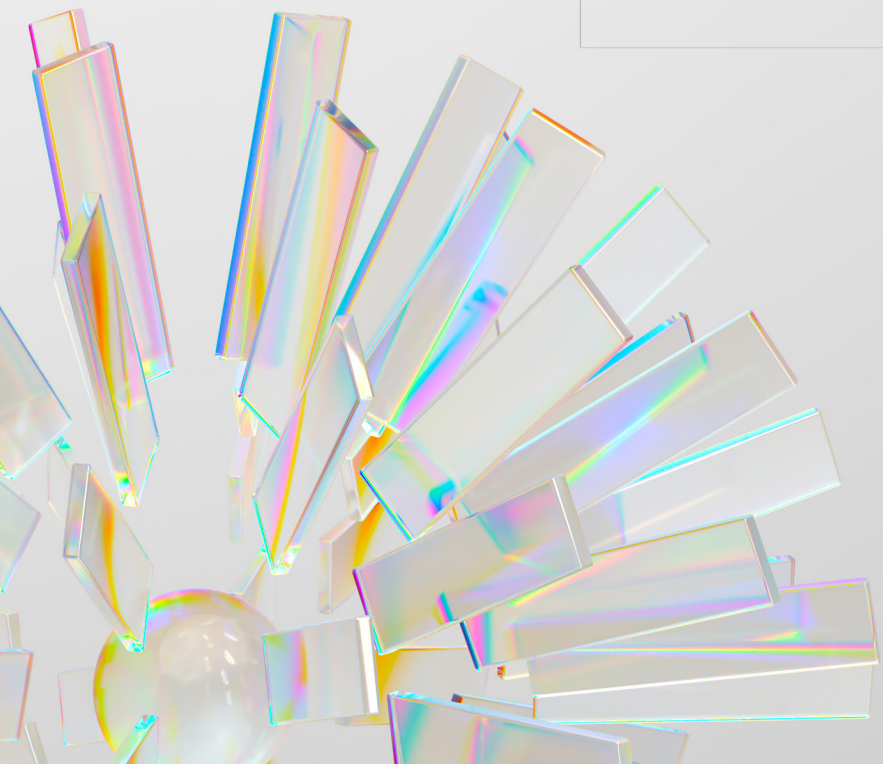
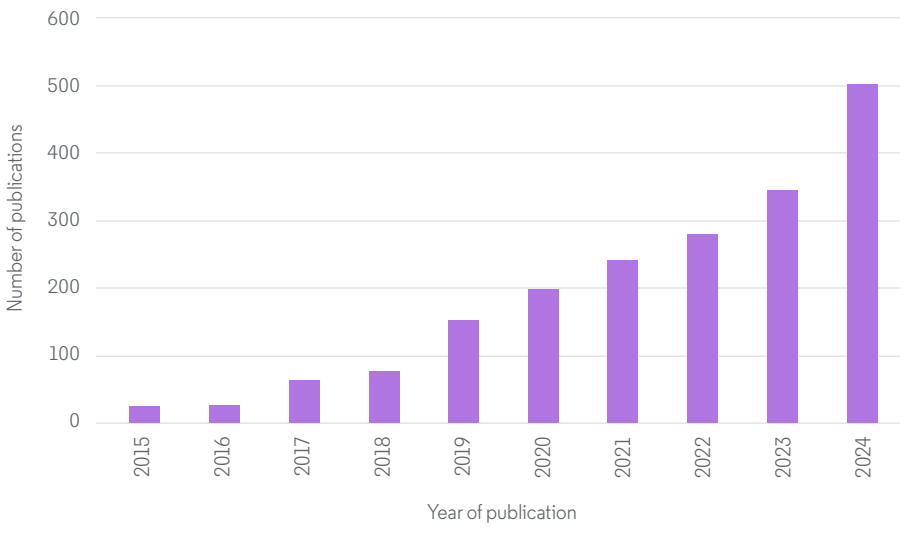


Foreword

Protein degraders have captured the pharmaceutical industry's interest due to scientific breakthroughs and a deeper understanding of the mechanism of action and targets. Their promise to address difficult-to-treat targets, primarily in oncology but also for autoimmune, inflammatory, neurodegenerative and infectious diseases, makes them a desirable addition to enhance pharma pipelines. This report explores the driving factors behind big pharma's growing interest in protein degraders and identifies innovative biotech companies to watch that are addressing the challenges and opportunities in this field.

Over the past nearly 20 years, rapid progress in the development of proteolysis-targeting chimeras (PROTACs) and molecular glue degraders have made them the most widely investigated and advanced targeted protein degraders (Figure 1). However, issues such as the unpredictability of protein-protein interactions, cell permeability and stability, and limited oral bioavailability are driving more recent advances. In addition, computational modeling and artificial intelligence (AI) within discovery platforms are streamlining screening and optimization of new technologies, targets and delivery mechanisms. For example, the $6bn deal between XtalPi and DoveTree Medicines announced in August 2025 will combine the former's AI-based discovery platform and the latter's biological insights to select and validate potential first-in-class candidates, including potentially including molecular degraders, across oncology, immunology and inflammatory diseases, neurological disorders and metabolic dysregulation (Chu, 2025).

Figure 1: The number of publications about PROTACs and molecular glue degraders has grown substantially year over year during the last 10 years



Source: Cortellis Drug Discovery Intelligence

Recent high-value deals in the space include the collaboration and option-to-license agreement between Magnet Biomedicine and Eli Lilly and Co for novel molecular glue degraders around oncology targets, which is worth up to $1.25bn and was announced in February 2025. This follows an active 2024, which featured nearly 20 deals totaling more than $13bn, highlighting pharma's interest in their potential.

The collaborative nature of many of these deals reflects the early stage of many protein degraders. They also highlight the interest from established large pharma to tap into clinically meaningful therapies for undruggable targets being developed by small, innovative biopharma companies, many of which were established in the last five years and are developing robust proprietary discovery platforms.

Arvinas Inc and Pfizer submitted a new drug application (NDA) to the U.S. Food and Drug Administration (FDA) for vepdegestrant (ARV-471) in June 2025 for the treatment of ER-positive/HER2-negative *ESR1*-mutated advanced or metastatic breast cancer, which represents the furthest milestone achieved of the assets currently in clinical development.

Bristol Myers Squibb and Genentech, a member of the Roche group, also have PROTACs in phase 3 trials. Although these target well-known, well-validated targets like estrogen receptor (ER) in breast cancer and androgen receptor (AR) in prostate cancer, they are helping to establish robust safety and efficacy results that can serve as a foundation for other therapies in earlier phases of development.

This report also identifies key areas of innovation, which are also driving interest in non-oncologic targets, including the AR for androgenetic alopecia, for which an asset from Kintor Pharmaceutical Ltd met its primary endpoint in its phase 2 trial.

Protein degrader therapies represent a significant opportunity for big pharma to address unmet patient needs. The convergence of scientific advancements, clinical success and innovative solutions from biotech companies is propelling the field forward. As concerns around efficacy and safety are addressed, protein degraders are poised to become a cornerstone of precision medicine, offering new hope for patients with difficult-to-treat diseases and conditions.

Protein degrader therapies represent a significant opportunity for big pharma to address unmet patient needs.

Achieving commercial success requires resilience in the face of obstacles

Although their mechanism wasn't fully understood at the time, protein degraders have been in the market for nearly 70 years. Thalidomide, a molecular glue, is perhaps the best-known example, although its molecular target and mechanism of action were only uncovered in the past two decades. Early efforts at developing targeted protein degraders over the last 20 years have faced hurdles in demonstrating proof of concept. Only recently has a critical mass of molecules advanced into late-stage development.

While enthusiasm is high, the field is still young. Unexpected clinical findings, variability in patient response and challenges translating preclinical efficacy into the clinic continue to shape development strategies. This history highlights the challenges pharma companies face across the development and commercialization lifecycle and what they should consider when acquiring and developing targeted protein degraders.

Clinical

Optimizing degrader design

Selecting the appropriate combination of components is crucial to selectivity and potency. Achieving the right balance of pharmacokinetics, oral bioavailability and stability can be complex and resource-intensive, requiring novel chemistry and screening approaches.

Target selection and biology

Identifying proteins that are both therapeutically relevant and susceptible to degradation remains a central challenge. Tumor heterogeneity, compensatory signaling pathways and incomplete understanding of degrader biology can limit efficacy. Biomarker discovery and patient stratification will be critical to realizing the clinical potential of this modality.

Clinical development

Designing and executing clinical trials for targeted protein degraders present unique challenges, including patient selection, dosing optimization and combination strategies. Addressing these challenges requires close collaboration with regulatory authorities and clinical investigators to ensure robust clinical trial design and execution.

Safety

Because targeted protein degraders often exploit novel mechanisms of action, predicting and managing on- and off-target effects is challenging. Clinical trial design must carefully account for safety monitoring, dose optimization and resistance mechanisms.

Regulatory

Evolving regulatory guidance

Because targeted protein degraders are still a relatively new therapeutic class, a standardized regulatory pathway is lacking. Companies must work closely with regulatory agencies to align on trial design, endpoints and approval requirements.

Addressing safety data expectations

Off-target degradation and downstream effects may not be fully predictable, and the effects could extend well beyond treatment discontinuation. It is important to be familiar with the latest guidance to meet expectations regarding pharmacokinetic, pharmacodynamic and toxicology data.

Biomarker development and patient stratification

Regulators will likely expect robust biomarker data to support efficacy claims. Identifying reliable biomarkers to demonstrate target engagement, degradation efficiency and patient selection will be important.

Market access and acceptance

Limited clinical experience

In the absence of previous experience with targeted protein degraders, uncertainty around long-term outcomes, durability of response and safety profiles may slow adoption by physicians and regulators alike.

Crowded market

Many of the therapies in late-stage development use the same target (e.g., AR or ER), which could create challenges regarding differentiation as they enter the market. In addition, clinicians may be more comfortable with proven treatments such as kinase inhibitors and monoclonal antibodies. Convincing stakeholders to switch to a new class will require strong clinical and economic evidence.

Availability of companion diagnostics and biomarkers

Market adoption will likely depend on identifying patient populations most likely to benefit. Lack of access to testing for validated biomarkers or diagnostics can create hurdles for payer acceptance and physician confidence.

Supply, manufacturing and distribution

Supply chain vulnerability
Dependence on specialized reagents, ligands or intermediates can expose companies to supply chain bottlenecks or geopolitical disruptions, especially given global reliance on limited suppliers.

Manufacturing consistency and quality control
Ensuring batch-to-batch reproducibility, stability and purity is critical, as minor variations in linker chemistry or ligase binders can affect efficacy and safety.

Financial

High R&D costs and long timelines
Designing degraders requires novel chemistry, screening and validation methods, which increase early-stage R&D expenses. Longer development cycles may also delay potential returns.

Competition for capital
As multiple companies enter the space, competition for venture funding, partnerships and licensing deals intensifies, driving up costs and diluting returns.

Intellectual property (IP)

Composition of matter patents
Protecting the specific chemical structures of degraders (e.g., PROTACs, molecular glues) is central, but the small-molecule-like nature of many degraders makes it challenging to secure broad, enforceable claims.

Patent life and exclusivity
As degraders advance slowly through clinical development, managing patent expiry timelines and extending exclusivity (e.g., through formulation, delivery or new-use patents) becomes critical for protecting investment.

Addressing these challenges requires a strategic approach that includes continuous investment in R&D, effectively navigating the regulatory landscape, engaging with stakeholders, interdisciplinary collaboration and transparent communication with the public. By overcoming these obstacles, companies can harness the transformative potential of targeted protein degraders to get effective therapies to the patients who need them.

Targeted protein degrader deals continue to rise

The increasing number and value of deals (Figure 2) underscore the strong interest from established pharmaceutical companies to access the potential of clinically meaningful therapies for undruggable targets being advanced by small, innovative biopharmas—many founded within the last five years and building robust proprietary discovery platforms. For these emerging players, partnerships provide critical resources to extend their operational runway and accelerate pipeline progress.

Figure 2: Number and value of deals for targeted protein degraders (2020—2024)

Source: Cortellis Drug Discovery Intelligence

The largest of the deals, between Evotec SE and Bristol Myers Squibb, represented an extension and expansion of their partnership established in 2018 between Evotec SE and Celgene, now BMS (Evotec, 2022). Potentially valued at $5bn, the companies agreed to another 8-year collaboration given their prior success at developing a promising pipeline of molecular glue degraders (Table 1). In the agreement, Evotec's proprietary EVOpanOmics and EVOpanHunter platforms and AI/machine learning (ML)-based drug discovery and development platforms will be used by both companies, in combination with BMS's library of cereblon E3 ligase modulators (CELMoDs™). In April 2025, performance-based and program-based achievements triggered payments of $75m to Evotec SE as part of the deal (Evotec, 2025).

Table 1: Top 10 protein degrader deals by total potential value (2020—2024)

Principal	Partner	Deal type	Therapy area	Degrader type	Date	Potential value ($bn)
Evotec SE	**Bristol-Myers Squibb**	Development collaboration	Multiple	Molecular glue	05/11/2022	5.00
Nurix Therapeutics	**Seagen Inc (now Pfizer)**	Collaboration to develop a portfolio of degrader-antibody conjugates (DACs)	Oncology	DAC	09/07/2023	3.46
Proxygen	**Merck**	Research collaboration and licensing agreement	Multiple	Molecular glue	04/05/2023	2.55
Nurix Therapeutics	**Sanofi**	Discovery, development and commercialization agreement	Multiple	Heterobifunctional	01/09/2020	2.50
Arvinas Inc	**Pfizer**	Global development and commercialization collaboration	Oncology	PROTAC	07/22/2021	2.40
Monte Rosa Therapeutics Inc	**Novartis**	Development and commercialization license agreement	Multiple	Molecular glue	10/28/2024	2.25
Kymera Therapeutics Inc	**Sanofi**	Development and commercialization agreement	Immune-inflammatory diseases	Molecular glue	07/09/2020	2.15
Monte Rosa Therapeutics Inc	**Roche**	Collaboration and licensing agreement	Neurology, oncology	Molecular glue	10/17//2023	2.05
Orionis Biosciences	**Genentech Inc, a member of the Roche Group**	Collaboration agreement	Neurology, oncology	Molecular glue	09/20/2023	2.05
Cullgen Inc	**Astellas Pharma Inc**	Research collaboration and exclusive option agreement	Unspecified	Heterobifunctional	06/15/2023	2.02

Source: BioWorld, Cortellis Deal Intelligence

In 2024, Nurix Therapeutics Inc extended its ongoing research collaboration with Gilead Sciences by an additional two years, earning the company a potential $1.79bn, including a $45m upfront payment.

One of the protein degrader companies with a longer tenure, San Francisco-based Nurix Therapeutics Inc was founded in 2009 (originally as Kura Therapeutics) based on research from University of California (UC) Berkeley and UC San Francisco. Its largest deal from 2020 through 2024 was forged with Seagen (now Pfizer) for up to $3.46bn including a $60m upfront payment, to develop DACs for oncology.

In 2024, Nurix Therapeutics Inc extended its ongoing research collaboration with Gilead Sciences by an additional two years, earning the company a potential $1.79bn, including a $45m upfront payment. The collaboration, which began in June 2019 with a potential price tag of $2.35bn, involves the identification of multiple targeted protein degrader candidates using Nurix Therapeutics Inc's proprietary drug discovery platform DELigase (Nurix Therapeutics Inc, 2024a). The companies' first joint development candidate GS-6791 (NX-0479), an oral IRAK4 degrader, is being explored to treat rheumatoid arthritis and other inflammatory diseases and was licensed by Gilead Sciences in 2023.

Also in 2024, Nurix Therapeutics Inc and Sanofi agreed to extend their research collaboration, which was established in 2020, for an unspecified amount (Nurix Therapeutics Inc, 2024b). The original agreement was valued at a potential $2.5bn. Their research program centers around degrading signal transducer and activator of a transcription-6 (STAT6), which is a key drug target in type 2 inflammation in allergic conditions. For drug candidates resulting from their collaboration, Sanofi retains a licensing option, while Nurix Therapeutics Inc has the option to co-develop and co-promote other products for which it has exercised its option in the United States.

In third place by value, Proxygen's partnership with Merck, worth up to $2.55bn, centers around molecular glue degraders against targets of unmet medical need (Richards, 2023). This followed a strategic collaboration with Merck established in June 2022 for up to $554m to jointly identify and develop molecular glue degraders up to a clinical candidate stage (Proxygen, 2022).

According to BioWorld data, 2025 has also been a busy year for partnerships in the space, with the following deals (with disclosed amounts) announced as of August 2025:

- Orionis Biosciences and Genentech, a member of the Roche Group, for a collaboration to discover molecular glue degraders for oncology targets, worth up to $2.105bn (Landenberger, 2025c)
- Neomorph Inc and AbbVie for a collaboration and option -to-license agreement for novel molecular glue degraders targeting multiple oncology and immunology targets, worth up to $1.64bn (Landenberger, 2025b)
- Magnet Biomedicine and Eli Lilly and Co for an agreement to discover, develop and commercialize molecular glue therapies for oncology, worth up to $1.25bn (Carey, 2025)
- Kymera Therapeutics Inc and Gilead Sciences for an option and license agreement for a molecular glue degrader program targeting solid tumors, worth up to $750m (Landenberger, 2025a)

Renewing collaborations appears to be a trend in the protein degrader space, with the $2.105bn agreement between Orionis Biosciences and Genentech Inc, a member of the Roche Group, representing the second for the companies (Landenberger, 2025c). In September 2023, the companies agreed to discover molecular glue degraders for targets in major disease areas including oncology and neurodegeneration, for a value up to $2.05bn.

The Neomorph Inc/AbbVie deal represents the third $1bn+ deal announced by Neomorph within a year, and Magnet Biomedicine scored its deal with Eli Lilly and Co only 17 months after emerging from stealth with its Trueglue discovery platform.

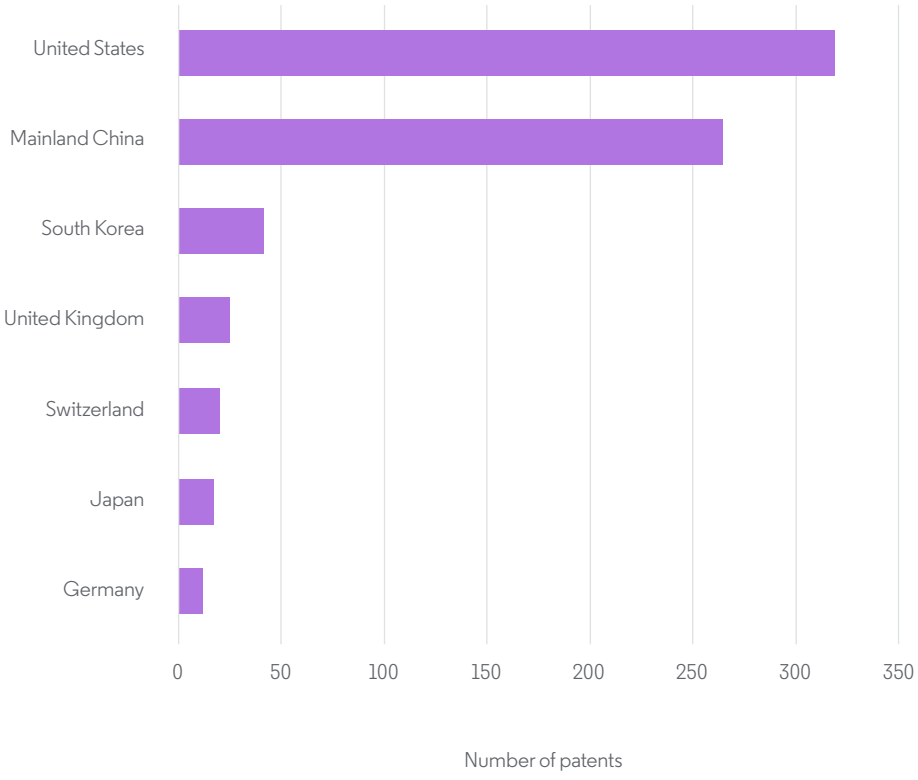
The field of targeted protein degraders is advancing rapidly

Innovation is also heating up, continuing to fuel interest in the potential of targeted protein degraders to fill gaps in pipelines and address unmet patient needs. The United States and Mainland China are in the clear lead in terms of patents and clinical trials (Figures 3 and 4).

Organizations in the United States filed 319 of the 717 patents (44.5%) globally for PROTACs, molecular glue degraders and E3 ligases over the past 10 years (according to Cortellis data). Organizations in Mainland China have filed 265, or 37% of the patents, for second position.

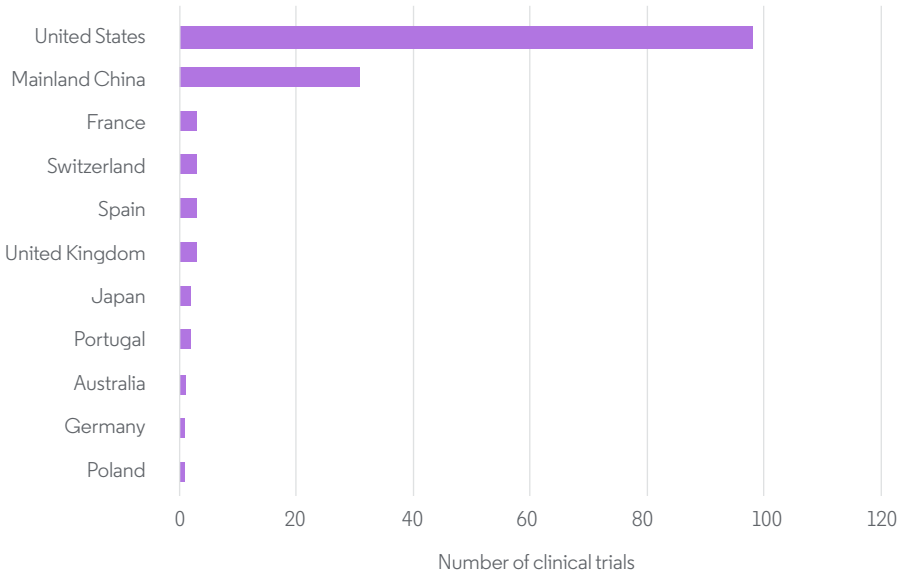
However, from 2020 through 2024, patents granted to companies Mainland China increased at an average annual rate of approximately 44%, surpassing those granted to companies in the United States during the same period (Clarivate, 2025).

Figure 3. Countries and regions (by company headquarters) leading innovation (>10 patents) in terms of patents filed globally for PROTACs, molecular glue degraders and E3 ligases (per first publication date; 2016-August 15, 2025)



Source: Cortellis Competitive Intelligence

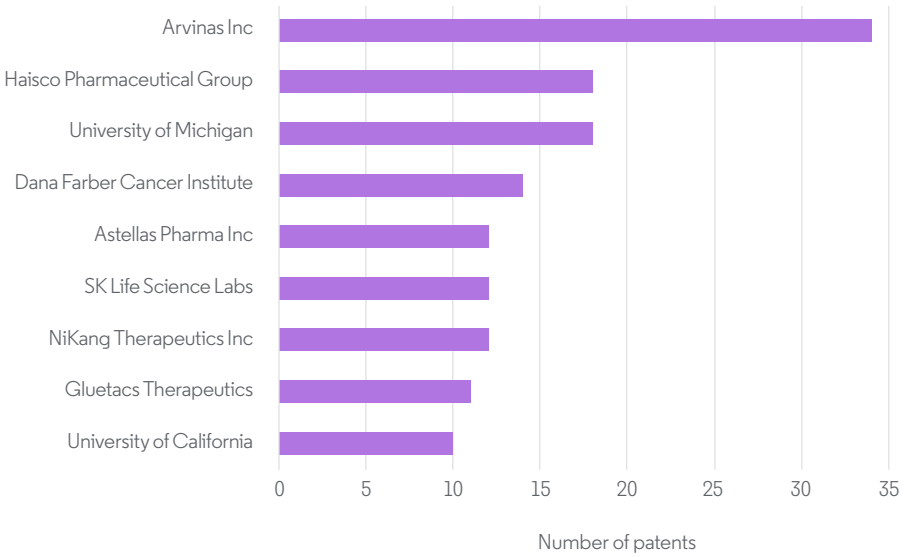
Figure 4. Countries and regions (by company headquarters) leading innovation in terms of clinical trials for PROTACs and molecular glue degraders started during the last 10 years (2016-August 15, 2025)



Source: Cortellis Clinical Trials Intelligence, clinicaltrials.gov

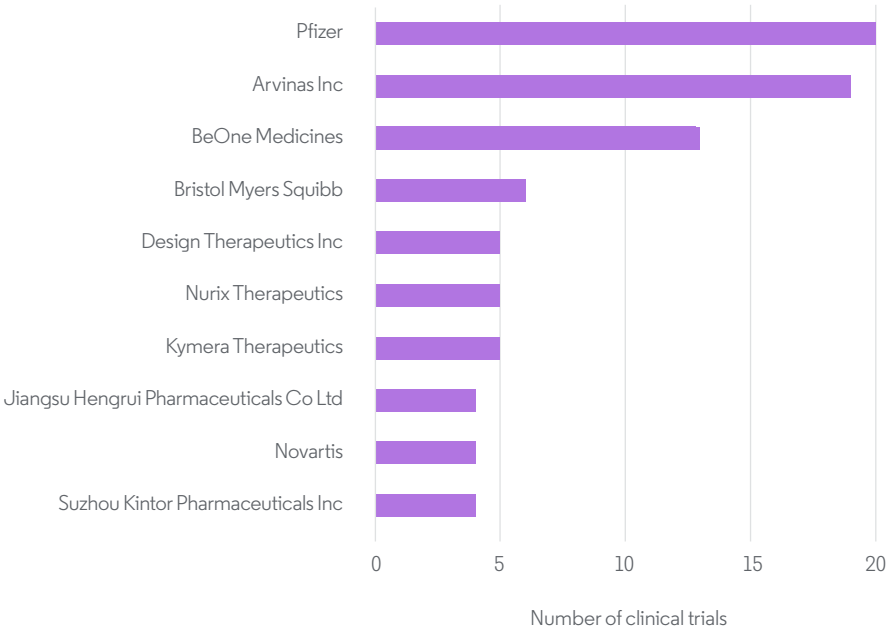
Regarding patents at the organization level, New Haven-based Arvinas Inc takes the lead (Figure 5), and it places second behind Pfizer for clinical trials started during the last 10 years (Figure 6). Its innovations have proven to be lucrative. In a worldwide development and commercialization agreement, Novartis committed to spend up to $1.09bn, including a $150m up-front payment, to access Arvinas Inc's PROTAC program, specifically RV-766, a second-generation PROTAC AR degrader for prostate cancer (Osborne, 2024).

Figure 5. Organizations leading innovation (>10 patents) in terms of patents filed globally for PROTACs, molecular glue degraders and E3 ligases (per first publication date; 2016-August 15, 2025)



Source: Cortellis Competitive Intelligence

Figure 6. Top 10 organizations leading innovation in terms of clinical trials for PROTACs and molecular glue degraders started during the last 10 years (2016-August 15, 2025)



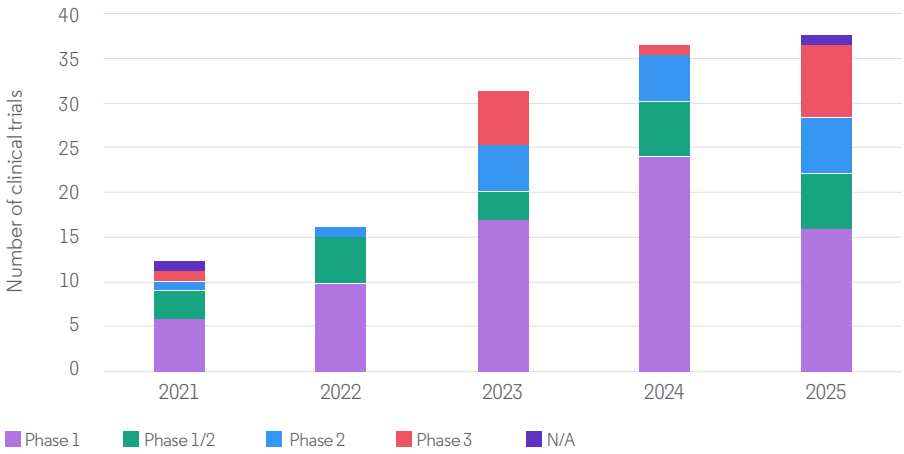
Source: Cortellis Clinical Trials Intelligence, clinicaltrials.gov

Arvinas Inc's latest-stage candidate, ARV-471 (vepdegestrant), is a PROTAC targeting ER and undergoing clinical testing for ER-positive breast cancer in partnership with Pfizer. Its PDUFA date has been set for June 5, 2026 (BioWorld, 2025d). Arvinas Inc has consistently demonstrated itself as a leader in the space, with its ARV-110 against metastatic castration-resistant prostate cancer as the first PROTAC to enter clinical trials in 2019 (Mullard, 2019).

The University of Michigan's recent degrader patent involves PROTACs comprising a von Hippel-Lindau disease tumor suppressor (VHL)-binding moiety and a STAT3-targeting moiety, which could be used across a range of indications (BioWorld, 2025a). Meanwhile, Haisco Pharmaceutical Group recently patented SMARCA2 degradation inducer PROTACs reported to be useful for lung cancer treatment (BioWorld, 2025c).

Much of the clinical development is still in early phases (Figure 7), although more PROTAC and molecular glue degrader assets are moving to phase 3 trials. This is especially true as some with established safety and efficacy are being explored for additional indications or combination treatment. For example, Novartis is conducting a phase 2 trial of luxdegalutamide in combination with abiraterone in adult male patients with metastatic hormone-sensitive prostate cancer, which began recruitment in July 2025.

Figure 7. Initiation of clinical trials for PROTACs and molecular glue degraders (as of August 15, 2025)

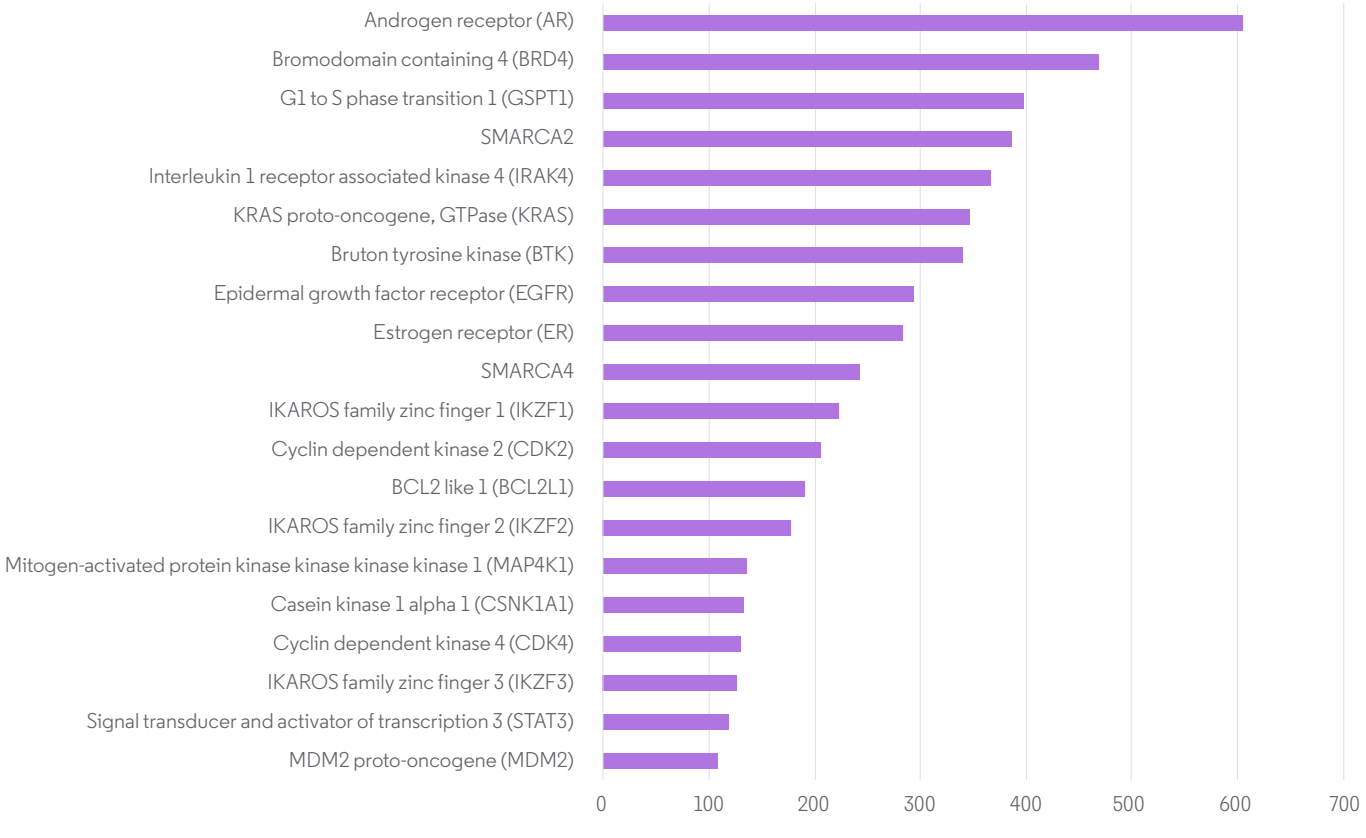


Source: Cortellis Clinical Trials Intelligence, clinicaltrials.gov

One noticeable trend with the compounds moving through later-phase trials is the selection of well-known, well-validated targets like AR (Figure 8 and Table 2).

This might reflect a strategic decision to potentially help address efficacy and safety concerns around protein degraders before companies progress to other, potentially more risky targets.

Figure 8: Top 20 targets in terms of PROTACs, molecular glue degraders and DACs being developed to target them



Source: Cortellis Drug Discovery Intelligence

Table 2. Examples of protein degraders in phase 3 development (as of August 25, 2025)

Molecule	Degrader type	Target	Indication	Companies	Phase
Bavdegalutamide (ARV-110)	PROTAC	Androgen receptor	Prostate cancer	Arvinas Inc	3
Luxdegalutamide (ARV-766)	PROTAC	Androgen receptor	Prostate cancer	Arvinas Inc	3
Vepdegestrant (ARV-471)	PROTAC	Estrogen receptor	Breast cancer	Arvinas Inc and Pfizer	3
BGB-16673	PROTAC	BTK	Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	BeOne Medicines	3
Gridegalutamide (BMS-986365/ CC-94676)	PROTAC	Androgen receptor	Prostate cancer	Bristol Myers Squibb	3
Giredestrant (GDC-9545)	PROTAC	Estrogen receptor	Breast cancer	Genentech, a member of the Roche Group	3

Source: BioWorld, Cortellis Clinical Trials Intelligence, clinicaltrials.gov, company websites

Molecular glue degraders bring target proteins and ubiquitin ligases close together, promoting the formation of protein complexes that otherwise would not interact and without needing a druggable binding pocket. Due to their smaller size, they are easier to administer orally than PROTACs. In contrast, PROTACs, first proposed in 2001, are larger heterobifunctional molecules that use a linker to connect ligands, one of which binds to the target protein while the other recruits E3 ubiquitin ligases to mark the protein for destruction.

Next-gen degraders are in development that promise to overcome some of the common design challenges with molecular glue degraders and PROTACs, such as the reliance on unpredictable protein-protein interactions for molecular glue degraders and challenges with cell permeability, metabolic stability and oral bioavailability for PROTACs due to their size and structural complexity.

These include DACs, which build on antibody-drug conjugate (ADC) experience and swap in degrader payloads. DACs could provide a favorable alternative by minimizing the need to achieve appropriate oral bioavailability, metabolic stability and plasma binding. Bristol Myers Squibb acquired the DAC BMS-986497 from Orum Therapeutics and is progressing it through phase 1 for acute myeloid leukemia. The phase 1 DAC ORM-502 is being evaluated by Orum Therapeutics for HER2-expressing advanced solid tumors.

Lysosome-targeting strategies are also gaining traction, including approaches targeting the endosome-lysosome pathway such as Lycia Therapeutics' lysosome-targeting chimeras (LYTACs) being developed for IgE-mediated diseases as well as Graves' disease (BioWorld, 2025b) or the autophagy-lysosome pathway such as AUTOTAC Bio Inc's autophagy-targeting chimera (AUTOTAC) in development for cancers (BioWorld, 2024). These emerging technologies can degrade targets not degradable by PROTACs, including extracellular proteins, organelles and non-protein autophagy substrates, because not all disease-relevant proteins can be degraded through the ubiquitin–proteasome system.

Outside of oncology, early-stage assets are being investigated for Parkinson's disease and progressive supranuclear palsy (ARV-102, a PROTAC from Arvinas Inc), allergic and atopic diseases (KT-621, a PROTAC from Kymera Therapeutics) and autoimmune diseases (MRT-6160, a molecular glue from Monte Rosa Therapeutics Inc and Novartis).

Next-gen degraders are in development that promise to overcome some of the common design challenges with molecular glue degraders and PROTACs.

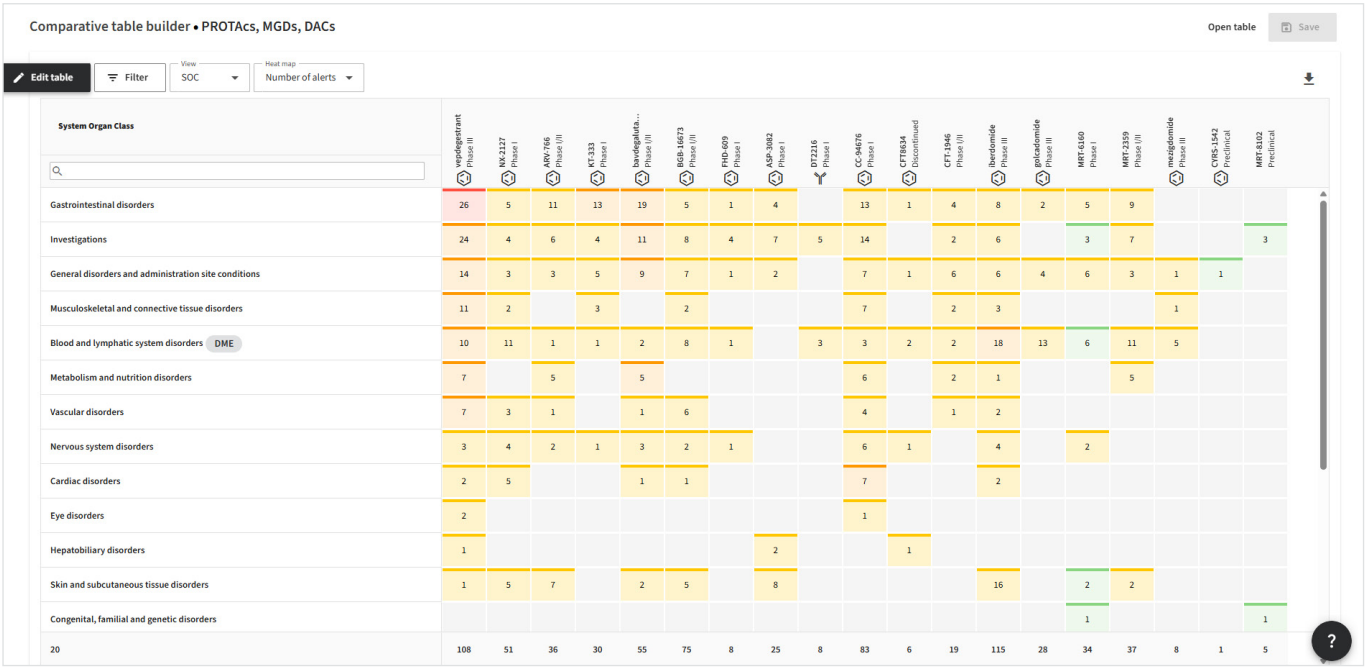
The regulatory landscape for degraders is beginning to take shape

As assets move through clinical development and are submitted for approval, expectations from regulatory agencies will become clearer. For now, vepdegestrant, the oral PROTAC degrader of ER from Arvinas Inc and Pfizer, is the most advanced of the modern targeted protein degraders. Its its NDA for ER-positive/HER2-negative *ESR1*-mutated advanced or metastatic breast cancer was accepted by the FDA on August 12, 2025, and the PDUFA date was set for June 5, 2026 (BioWorld, 2025e).

The submission was based on results from VERITAC-2, a global phase 3 trial evaluating vepdegestrant versus fulvestrant that demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS; median 5 months with vepdegestrant vs 2.1 months with fulvestrant) and reduced the risk of disease progression or death by 43% compared with fulvestrant (Arvinas Inc, 2025).

Although the first approved degrader, thalidomide, was famously associated with birth defects, a greater understanding of the mechanism of action and affected pathways has resulted in improved safety profiles for currently developed protein degraders (Figure 9). In the VERITAC-2 trial, vepdegestrant's safety profile involved mostly low-grade treatment-emergent adverse events (TEAEs). The three most common were fatigue (26.6%), increased alanine transaminase (ALT) levels (14.4%) and increased aspartate aminotransferase (AST) levels (14.4%). Treatment discontinuation for TEAEs occurred for 2.9% of patients taking vepdegestrant, compared with 0.7% of patients taking fulvestrant.

Figure 9: Comparative evaluation of adverse events for a selection of PROTACs, molecular glues and DACs

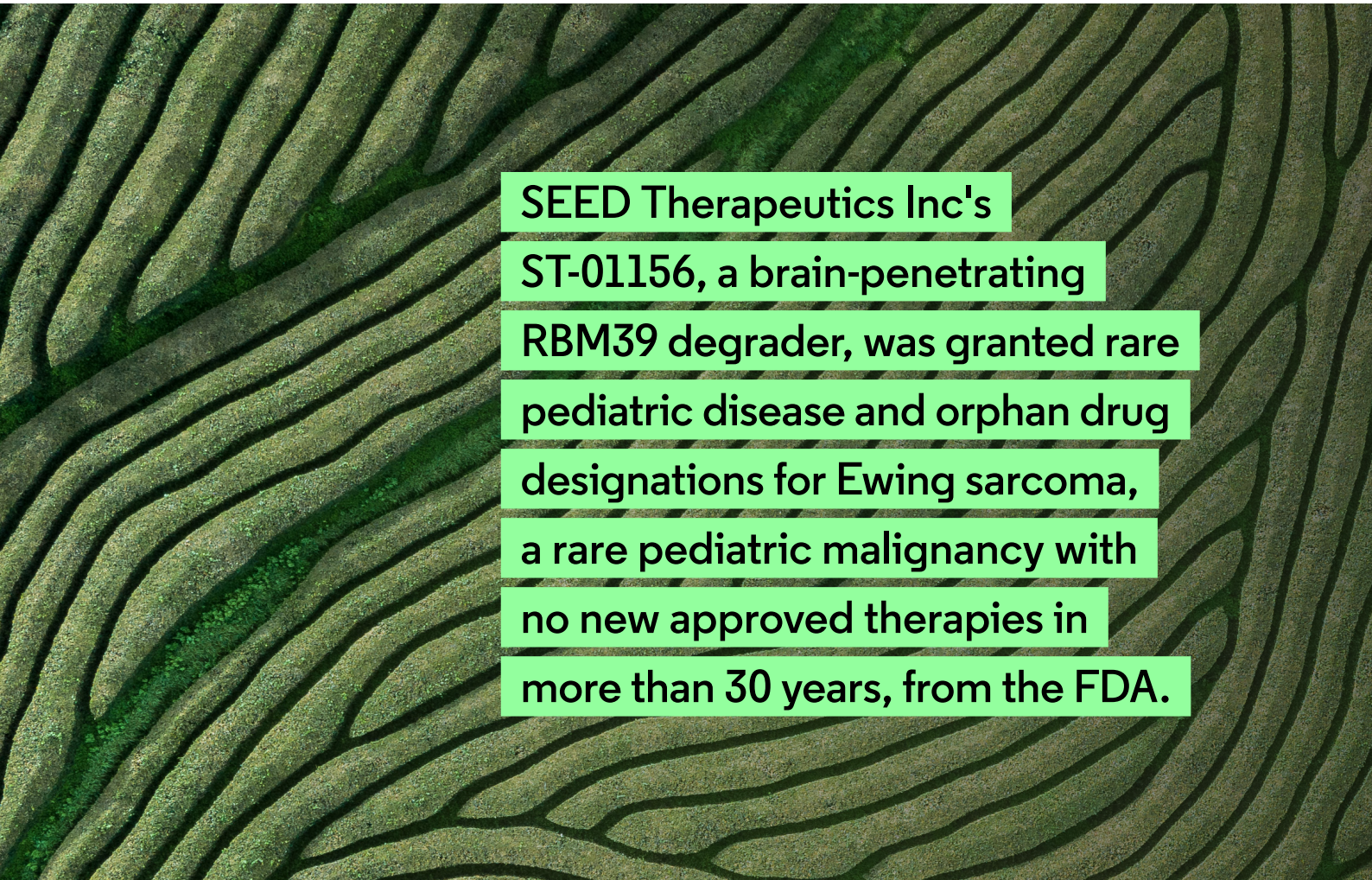


Source: OFF-X

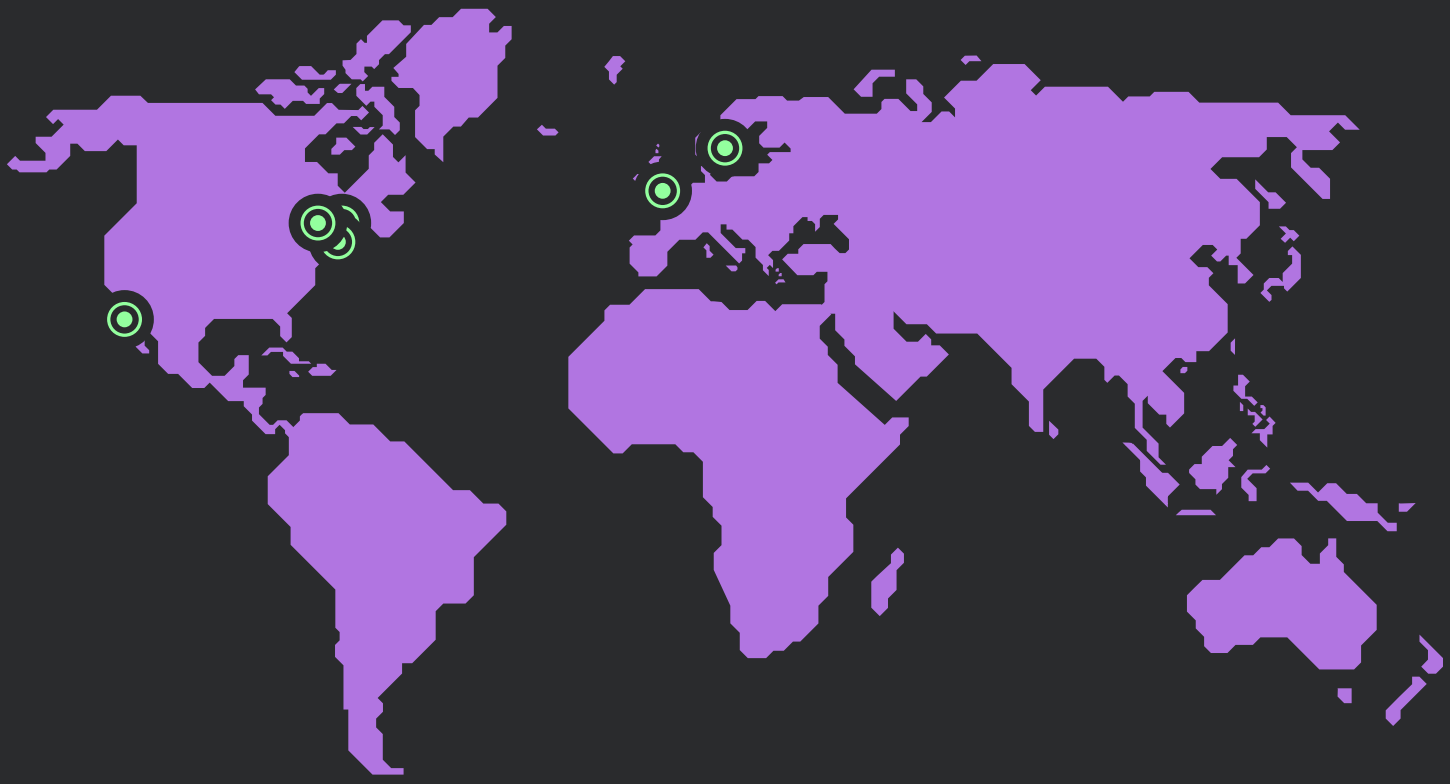
Given that targeted protein degraders typically address rare or difficult-to-treat conditions, many are benefitting from accelerated approval pathways from the FDA and European Medicines Agency (EMA). For example, Nurix Therapeutics Inc's bexobrutideg (NX-5948), a phase 1/2b PROTAC targeting Bruton's tyrosine kinase (BTK) for non-Hodgkin's lymphoma (NHL), including CLL and SLL as well as Waldenstrom macroglobulinemia (WM), was granted U.S. FDA fast track designation (January 2024) and EMA PRIME designation (November 2024) for CLL and SLL as well as FDA and EMA orphan drug designations for WM (March 2025 and July 2025, respectively; BioWorld, 2025f).

Similarly, the BTK degrader BGB-16673 from BeOne Medicines was granted EMA PRIME designation for WM in July 2025. It is currently in phase 3 for CLL and phase 2 for mantle cell lymphoma (MCL), WM and B-cell malignancies (in combination with zanubrutinib and sonrotoclax).

In addition, in January 2025, SEED Therapeutics Inc's ST-01156, a brain-penetrating RBM39 degrader, was granted rare pediatric disease and orphan drug designations for Ewing sarcoma, a rare pediatric malignancy with no new approved therapies in more than 30 years, from the FDA. Originating from the company's proprietary RITE3™ platform, ST-01156 is SEED Therapeutic Inc's first clinical candidate, and recruitment for the phase 1 trial is expected to commence in Q1 2026 (SEED Therapeutics Inc, 2025).



Companies to watch



Beactica Therapeutics AB

Uppsala, Sweden

Per Källblad,
Helena Danielson

Kymera Therapeutics

Watertown, Massachusetts

Nello Mainolfi

Monte Rosa Therapeutics

Boston, Massachusetts

Rajesh Chopra,
Ian Collins

Nurix Therapeutics Inc

Brisbane, California

John Kuriyan,
Michael Rapé,
Arthur Weiss

TRIANA Biomedicines

Lexington, Massachusetts

N/A

TRIMTECH Therapeutics

Cambridge, UK

Cambridge Innovation Capital (CIC) and SV Health Investors' Dementia Discovery Fund (DDF), in collaboration with Damian Crowther, Leo James and Will McEwan

Beactica Therapeutics

Beactica Therapeutics AB is a privately held precision medicine company that was founded as a spin-out from Uppsala University. Its pipeline of novel small molecule therapeutics is advanced to treat diseases with significant unmet medical need. Beactica's approach is centered around its Eclipsor™ platform, which was designed to enable the efficient development of allosteric modulators and targeted protein degraders. Beactica aims to deliver value to patients and shareholders by advancing its programs to clinical proof of concept.

Company profile

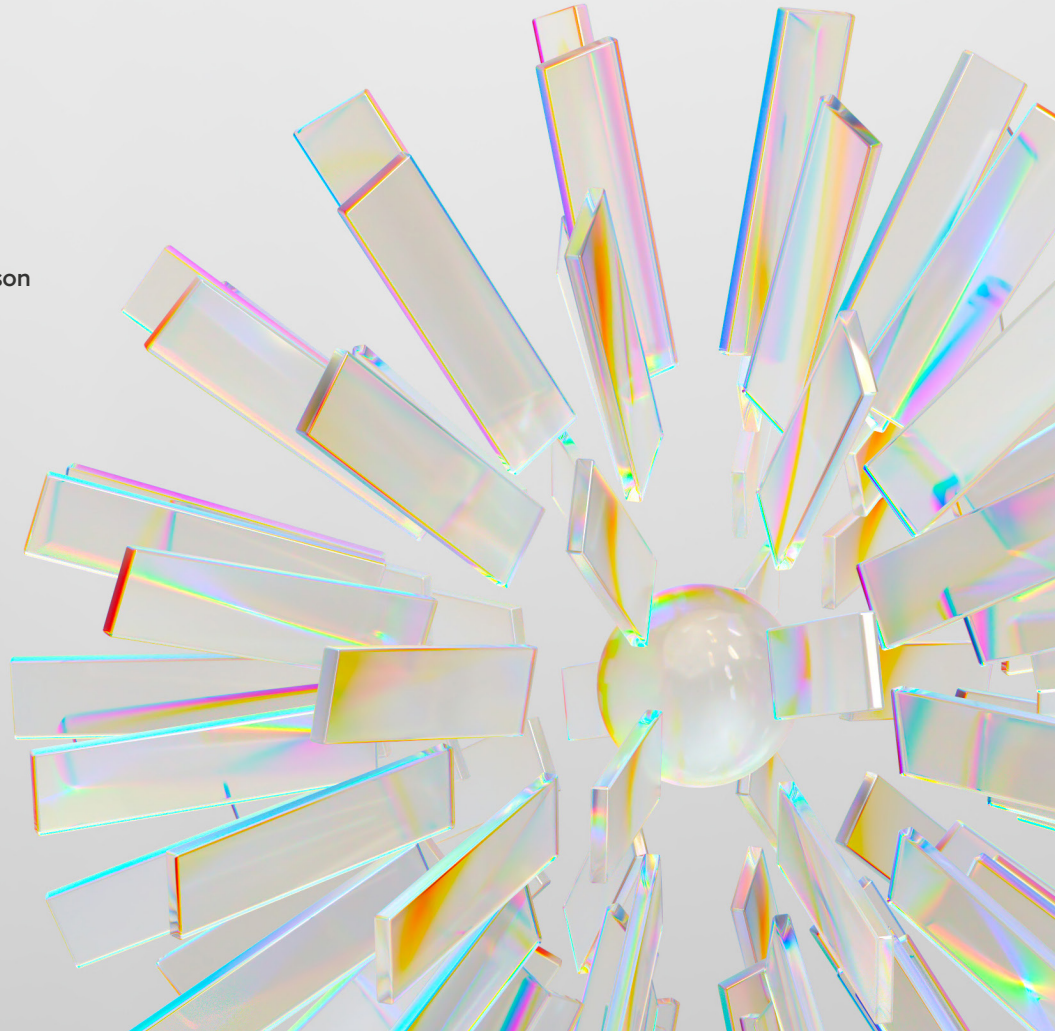
Founded: **2006**

Founders: **Per Källblad, Helena Danielson**

Headquarters: **Uppsala, Sweden**

Investors

- Private equity and family offices



Partners

Academic

Uppsala University
Research collaboration involving novel allosteric modulator/degrader of lysine specific demethylase 1 (LSD1)–CoREST under development by Beactica for treatment of cancer.

Karolinska Institute
Research collaboration involving novel allosteric modulator/degrader of LSD1–CoREST under development by Beactica for treatment of cancer.

KU Leuven
Research collaboration involving novel allosteric modulator/degrader of LSD1–CoREST under development by Beactica for treatment of glioblastoma (GBM).

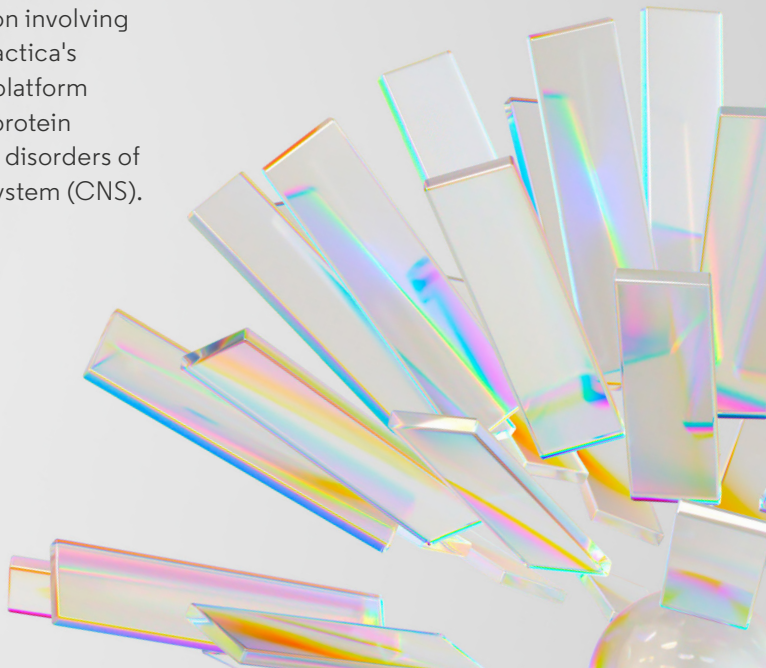
MD Anderson Cancer Center
Research collaboration involving novel bifunctional proteolysis-targeting degraders of transcriptional enhanced associate domain (TEAD) under development by Beactica for treatment of cancer.

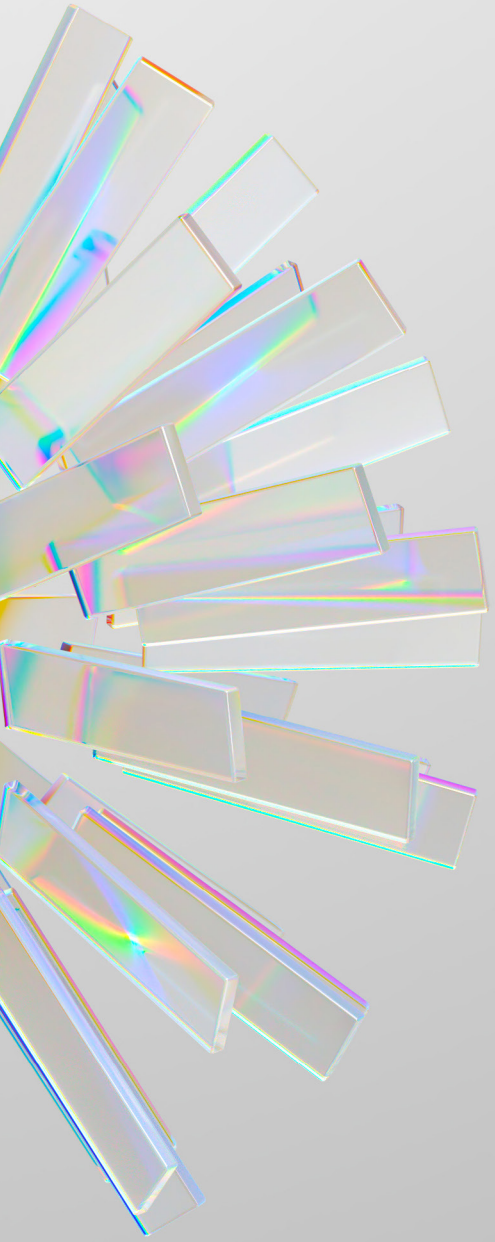
National Center for Advancing Translational Sciences (NCATS), U.S. National Institutes of Health (NIH)
Research collaboration involving novel bifunctional proteolysis-targeting degraders of TEAD under development by Beactica for treatment of cancer.

The Broad Institute of MIT and Harvard
Research collaboration involving novel bifunctional proteolysis-targeting degraders of TEAD under development by Beactica for treatment of cancer.

Corporate

BioArctic
Research collaboration involving the application of Beactica's Eclipsor technology platform to develop targeted protein degraders to address disorders of the central nervous system (CNS).





What makes this company stand out?

- Beactica Therapeutics has a proven track record spanning more than 15 years of successfully delivering pharmaceutical innovation using its Eclipsor platform to address challenging targets across diverse therapeutic areas. Examples in the public domain include the world's first inhibitor of USP7 (outlicensed by Almac to Genentech in a $349m deal) and novel allosteric modulators of the alpha-7 nicotinic acetylcholine receptor (Spurny et al, 2015).
- Beactica aims to develop a pipeline of first-in-class or best-in-class allosteric modulators/degraders and bifunctional targeted protein degraders with the potential to change the prospects for patients with life-threatening diseases.
- Beactica's BEA-17, an oral LSD1–CoREST degrader that has the potential to be first in class for glioblastoma, could reverse immune evasion, boost antigen presentation, trigger viral mimicry and shift macrophages to pro-inflammatory states.
- Beactica has successfully established a network including leading universities and institutes that enables it to access relevant, up-to-date expertise and knowledge in the fast-moving field of molecular medicine.

How will the company's solution benefit patients and their caregivers?

- Beactica Therapeutics' vision is to create breakthrough therapeutics that transform the prospects for patients with life-threatening diseases. To achieve this, the company focuses on indications and targets where it believes its Eclipsor platform offers a competitive advantage and there is a high unmet medical need in well-defined patient populations.
- GBM remains highly lethal due to profound immune evasion and a lack of effective treatments. BEA-17 has the potential to significantly increase patients' life expectancies in a very aggressive disease.

Funding and grants

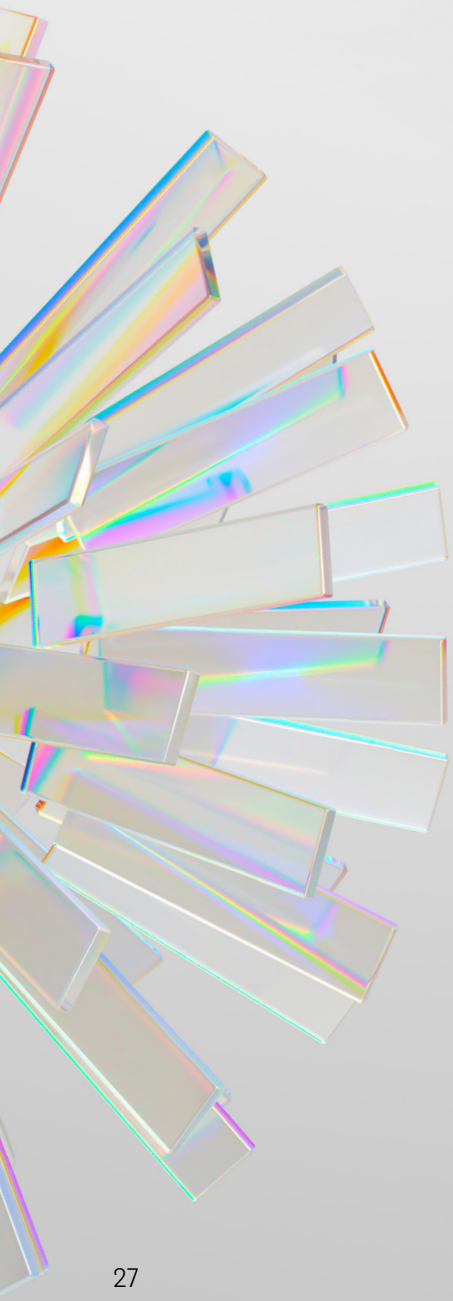
- Equity funding ($12.5m in total)
- Grant funding ($4.5m in total)

IP status and patent filings

- Beactica's IP strategy is focused on establishing strong intellectual property protection for its drug candidates in all major geographical markets.
- Patent applications have been filed for novel allosteric modulators/degraders of LSD1–CoREST under development by Beactica for treatment of diseases such as cancer.
- Patent applications have been filed for novel bifunctional proteolysis-targeting degraders of TEAD under development by Beactica for treatment of diseases such as cancer and fibrosis.

R&D activity

- BEA-17 is progressing to phase 1 studies for GBM:
  - Preclinical development is underway to enable biomarker-driven clinical translation and position it at the forefront of immuno-epigenetic therapies for GBM.
  - It was granted orphan drug designation for the treatment of GBM by the U.S. FDA.
- Indication selection is underway for P65-047, a novel bifunctional proteolysis-targeting degrader of TEAD transcription factors:
  - P65-047 has shown superior efficacy over competitor compounds across several human cancer types.
  - It has achieved significant and dose-dependent elimination of TEAD1 in the target tissue.
  - Its efficacy is correlated with VGLL3-regulated transcription, which is noteworthy as overexpression of VGLL3 is associated with poorer patient outcomes in several cancers with significant unmet medical need.
- Additional degrader programs driven by the Eclipsor technology platform are in early-stage research for undisclosed targets.



"Beactica doesn't just discover new compounds, we precision engineer them. Our validated Eclipsor™ platform produces novel allosteric modulators and targeted protein degraders. This gives us a unique edge in addressing challenging disease proteins where others see limits. Our track record of successfully delivering pharmaceutical breakthroughs for the benefit of patients, spanning more than 15 years, is something that we are very proud of."

Per Källblad,
PhD, Beactica Therapeutics Co-Founder and CEO

Kymera Therapeutics

Kymera is a clinical-stage biotechnology company developing targeted protein degradation medicines that address critical health problems and have the potential to dramatically improve patients' lives. Kymera is deploying targeted protein degradation to address disease targets and pathways often inaccessible with conventional therapeutics. Having advanced the first degrader into the clinic for immunological diseases, Kymera is focused on building an industry-leading pipeline of oral small molecule degraders to provide a new generation of convenient, highly effective therapies for patients with these conditions.

Company profile

Founded: **2016**

Founders: **Nello Mainolfi**

Headquarters: **Watertown, Massachusetts**

Investors

- N/A (public company; Nasdaq: KYMR)

Partners

Academic	Corporate
Non-disclosed	**Gilead Sciences Inc** Collaboration agreement to develop an oral molecular glue degrader program that targets cyclin-dependent kinase 2 (CDK2) with broad oncology treatment potential including breast cancer and other solid tumors. **Sanofi** Collaboration agreement to develop oral small molecule IRAK4 protein degraders for immune-inflammatory diseases worldwide.

What makes this company stand out?

- Kymera is focused on developing targeted protein degraders against disease targets in areas of significant patient need that often cannot be meaningfully addressed by traditional medicines and where targeted protein degradation is potentially the only or best way to elucidate the desired biology or clinical outcome. This approach includes addressing historically undrugged proteins and broad pathways and nodes with strong genetic and clinical validation.
- Kymera's toolbox of integrated approaches was created to accelerate the discovery and development of transformative degrader medicines, enabling it to study molecular structures and gain a full understanding of the biological mechanisms of proteins including:
  - A comprehensive hit identification strategy using high-content as well as fit-for-purpose technologies such as DNA-encoded libraries and fragment and X-ray-based screenings.
  - ML and AI hit-validation and optimization technologies.
  - Structure (e.g., X-ray crystallography and cryogenic electron microscopy) and pharmacokinetic/pharmacodynamic-centric-enabled lead optimization.
  - Translational biology focused on patient disease samples.
- The company has generated and validated predictive models reflecting the interplay between targets and drug properties and that facilitate optimization of drug disposition and in vitro and in vivo pharmacokinetic/pharmacodynamic relationships of its degraders across different tissue and cell types.
- The company is also exploring the development of adjacent technologies and next-generation targeted protein degrader strategies to further expand the range of targets for degrader therapies.

How will the company's solution benefit patients and their caregivers?

- Kymera aims to revolutionize immunology with oral medicines, working to challenge long-standing paradigms with a unique mechanism of action, broad therapeutic potential and patient-friendly delivery.

- KT-621, which targets STAT6, the specific transcription factor responsible for IL-4/IL-13 signaling and the central driver of Th2 inflammation, has the potential to transform treatment paradigms for more than 130 million patients worldwide, including children and adults with Th2 diseases such as atopic dermatitis, asthma, chronic obstructive pulmonary disease (COPD), chronic rhinosinusitis with nasal polyps (CRSwNP), eosinophilic esophagitis (EoE), chronic spontaneous urticaria (CSU) and prurigo nodularis, among others.

- KT-579, which targets IRF5, a genetically validated transcription factor and master regulator of immunity, may selectively block inflammation and restore immune regulation by inhibiting pro-inflammatory cytokines, type I IFN and autoantibody production while sparing normal cell function. KT-579 has the potential to be the first novel mechanism with broad utility in diseases where effective and well-tolerated oral therapies are needed, such as lupus, Sjögren's, inflammatory bowel disease (IBD), rheumatoid arthritis (RA) and others.

Funding and grants

August 2020:
IPO ($200m); Nasdaq: KYMR

March 2020:
Series C financing ($102m)

November 2018:
Series B financing ($65m)

October 2017:
Series A financing ($30m)

IP status and patent filings

- Non-disclosed

R&D activity

Wholly owned programs:

- KT-621 is a once-daily, oral degrader of STAT6 that demonstrated complete STAT6 degradation in blood and skin following low daily oral doses, reductions in multiple disease-relevant Th2 biomarkers and a safety profile undifferentiated from placebo in the phase 1 clinical study with healthy volunteers.

- KT-579 is an oral degrader of IRF5 that demonstrated equal or greater efficacy than clinically active or marketed small molecule inhibitors and biologics in preclinical models of lupus and RA. In preclinical safety studies, KT-579 did not show any adverse effects of any type at the tested doses and concentrations.

Partnered programs:

- KT-485/SAR447971, a second-generation, selective, potent, oral IRAK4 degrader being advanced in partnership with Sanofi for immuno-inflammatory diseases, is in IND-enabling studies.

- An oral molecular glue degrader program targeting CDK2 for the potential treatment of solid tumors, developed in collaboration with Gilead, is currently in preclinical studies.

"By combining the 'right target' with the disruptive potential of targeted protein degradation, Kymera is delivering oral therapies with biologics-like profiles for the first time in industry with the potential to expand access to millions of patients around the world."

Nello Mainolfi,
PhD, Kymera Therapeutics Founder, President and CEO

Monte Rosa Therapeutics

Headquartered in Boston, Massachusetts, Monte Rosa Therapeutics was launched from Ridgeline, Versant's Discovery Engine based in the Basel Technology Park, and has research operations in both Boston and Basel, Switzerland. Monte Rosa's QuEEN™ (Quantitative and Engineered Elimination of Neosubstrates) discovery engine combines AI-guided chemistry, diverse chemical libraries, structural biology and proteomics to rationally design selective molecular glue degraders. Monte Rosa aims to develop the industry's leading pipeline of 'only-in-class' molecular glue degraders spanning autoimmune and inflammatory diseases, oncology and beyond, with three programs in the clinic.

Company profile

Founded: **2018**

Founders: **Rajesh Chopra, Ian Collins**

Headquarters: **Boston, Massachusetts**

Investors

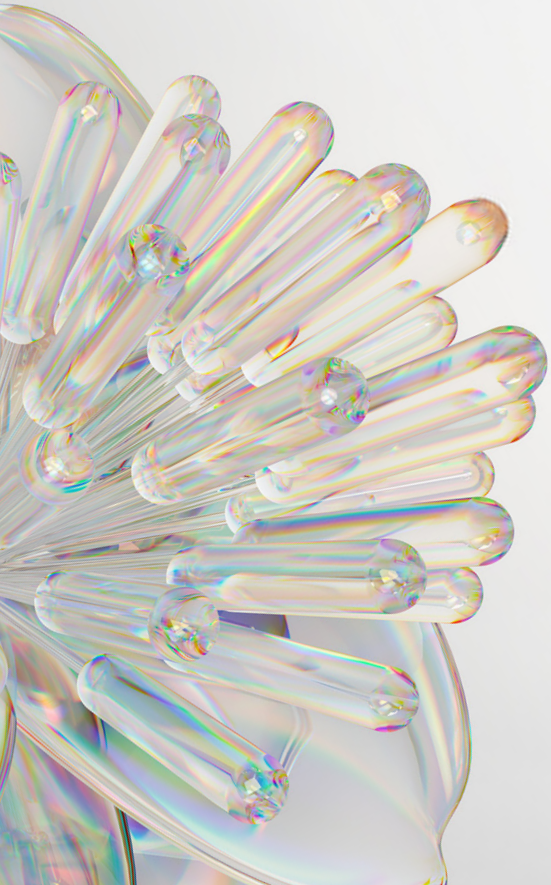
- New Enterprise Associates (NEA)
- T.Rowe Price Associates Inc
- BVF Partners L.P.
- Versant Ventures
- Baker Bros. Advisors L.P.
- Dimension Management L.P.
- Avoro Capital Advisors LLC
- Suvretta Capital Management LLC
- BlackRock Institutional Trust Company N.A.
- The Vanguard Group Inc
- Fidelity Institutional Asset Management
- Aisling Capital Management LP
- Alphabet Inc
- HBM Partners AG

Partners

Academic	Corporate
N/A	**Novartis** Global license agreement to advance VAV1- directed molecular glue degraders, including MRT-6160, to accelerate and broaden scope of clinical development for immune-mediated diseases.
	Roche Strategic collaboration to discover and develop novel molecular glue degraders, expanding platform reach to discover and develop molecular glue degraders against previously undruggable targets in cancer and neurological diseases.

What makes this company stand out?

- Monte Rosa has been exclusively focused on molecular glue degraders since its founding and has made addressing previously undruggable, high-value therapeutic targets a priority.
- Using its QuEEN discovery engine, Monte Rosa Therapeutics has made selective, catalytic molecular glue degraders that degrade disease-causing proteins and modulate disease pathways. QuEEN has helped generate a pipeline of molecular glue degraderss focused in the areas of immunology and inflammation, oncology and more.
- Since the beginning, Monte Rosa has believed the target space for molecular glue degraders is much larger than historically understood. A recent publication in Science (Petzold et al, 2025) details how Monte Rosa's proprietary AI and ML engine has uncovered a broad range of human proteins potentially accessible to cereblon-based degradation, spanning diverse protein domains and classes. These findings expand the actionable target space for molecular glue degrader drug discovery.
- The company's understanding and use of novel binding modes, extending beyond established degron surfaces, allows it to fine-tune selectivity and reach more targets.



How will the company's solution benefit patients and their caregivers?

- By degrading proteins that lack classical drug-binding pockets, the company aims to develop highly selective molecular glue degraders that address historically difficult or undruggable targets known to drive serious diseases.

Funding and grants

May 2024:
Underwritten public offering ($100m).

June 2021:
Initial public offering ($255.6m), trading on the Nasdaq Global Select Market under the ticker symbol GLUE.

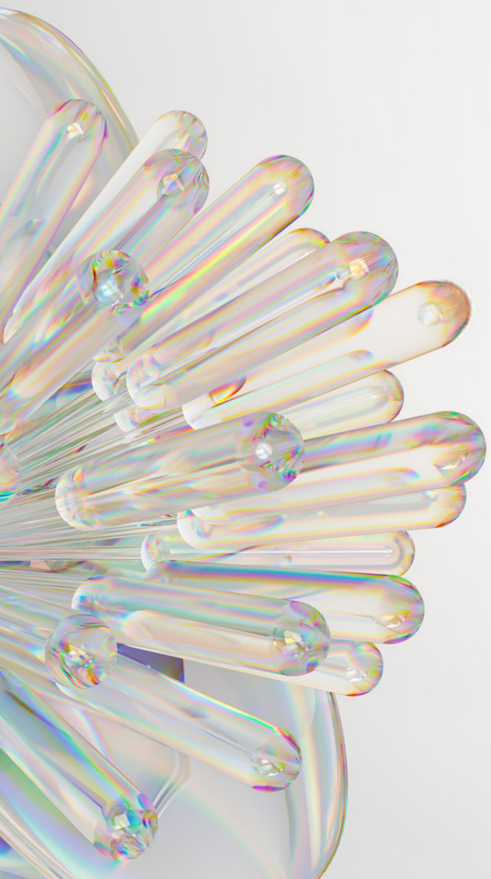
March 2021:
Series C financing ($95m), led by Avoro Capital Advisors with participation from Fidelity Management & Research Company LLC, funds and accounts managed by BlackRock, funds and accounts advised by T. Rowe Price Associates Inc, RTW Investments LP, Versant Ventures, New Enterprise Associates, Aisling Capital, Cormorant Asset Management, HBM Healthcare Investments, GV, Amzak Health, Sixty Degree Capital, Casdin Capital and Cambridge Asset Management.

September 2020:
Series B financing ($96m), led by Aisling Capital with participation from founding investor Versant Ventures, existing investor New Enterprise Associates, as well as HBM Healthcare Investments, Cormorant Asset Management, GV, Amzak Health, Casdin Capital, Sixty Degree Capital and Cambridge Asset Management.

May 2020:
Series A financing ($32.5m) from founding investor Versant Ventures and New Enterprise Associates.

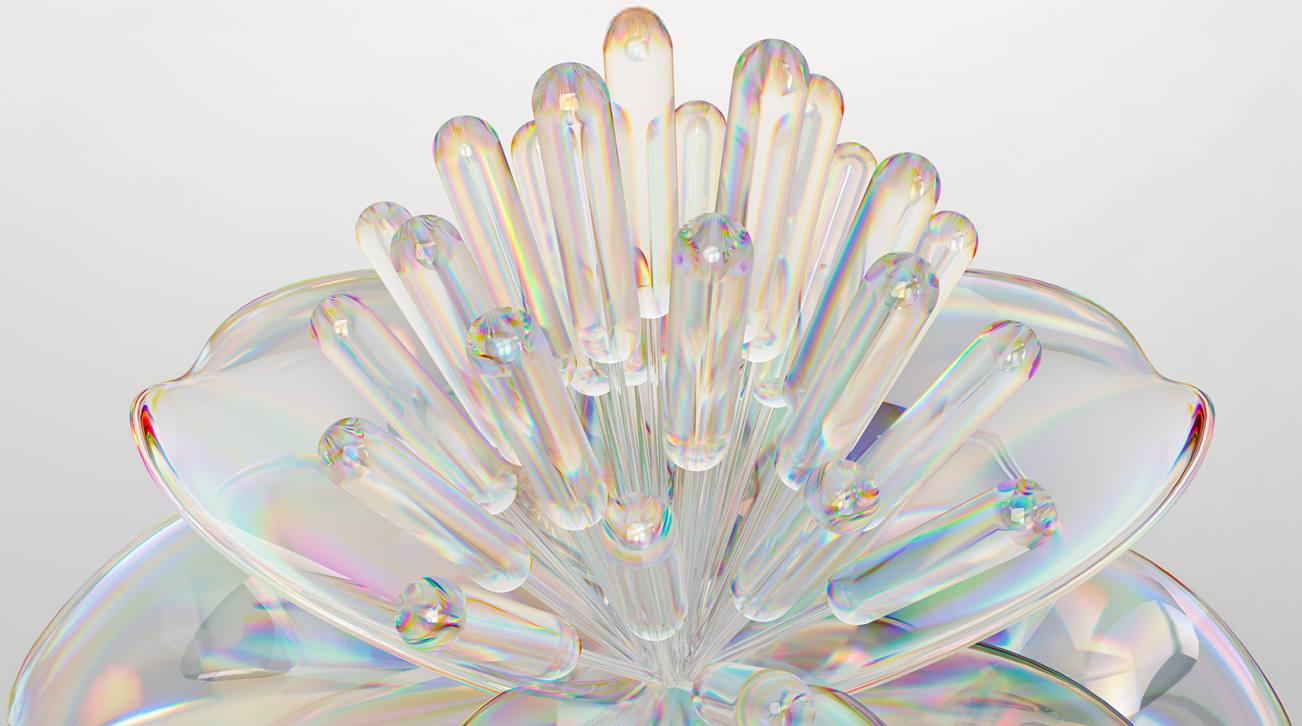
IP status and patent filings

- As of December 31, 2024, Monte Rosa owned 39 patent families related to its QuEEN discovery engine; the programs CCNE, CDK2, NEK7, VAV1 and GSPT1; and GSPT1-directed molecular glue degraders and biomarkers related to these compounds.



R&D activity

- MRT-6160, a VAV1-targeted molecular glue degrader to treat immune-mediated diseases, is being advanced in collaboration with Novartis toward multiple phase 2 studies.
- MRT-8102, a NEK7-directed molecular glue degrader for inflammatory diseases driven by the NLRP3 inflammasome, IL-1β and IL-6, is in a phase 1 trial.
  - The ongoing study includes single ascending dose (SAD)/ multiple ascending dose (MAD) cohorts in healthy volunteers and an additional cohort designed to evaluate potential early proof of concept in participants with increased cardiovascular disease risk and elevated C-reactive protein (CRP).
  - Initial data are expected in H1 2026.
- GSPT1-directed molecular glue degrader MRT-2359 targeting MYC-driven solid tumors is in a phase 1/2 study.
  - The company is evaluating MRT-2359 in castration-resistant prostate cancer
  - Additional clinical data are expected to be reported later in 2025.
- Assets targeting CCNE1 and CDK2 for the treatment of solid tumors are both in preclinical development, and the company expects to submit an IND application for a CDK2 and/or cyclin E1-directed MGD in 2026.
- The company has multiple discovery-stage assets against targets for immunologic/inflammatory diseases, genetic diseases and neurologic diseases.



"At Monte Rosa, we have long believed that molecular glue degraders could redefine small molecule drug development by combining the advantages of large molecule modalities such as RNAi to eliminate a disease-causing protein with exquisite selectivity with all the benefits of orally available small molecule drugs. Our team has advanced an industry leading pipeline of MGDs, spanning immunology and inflammation, oncology, and more, and we have intentionally focused our efforts on previously undruggable targets. This work is a result of the strength of our amazing team, our unparalleled QuEEN™ drug discovery engine, and a firmly held conviction that molecular glue degraders are particularly well-suited to address many of today's most challenging targets and diseases."

Markus Warmuth,
MD, Monte Rosa Therapeutics CEO

Nurix Therapeutics Inc

Nurix Therapeutics is a clinical-stage biopharmaceutical company developing targeted protein degradation therapies powered by its AI-integrated DEL-AI discovery engine. In its diversified, partnered pipeline, Nurix is advancing a range of degrader and DAC candidates for oncology, autoimmune and inflammatory diseases, with a focus on high-value targets such as BTK, STAT6 and IRAK4.

Company profile

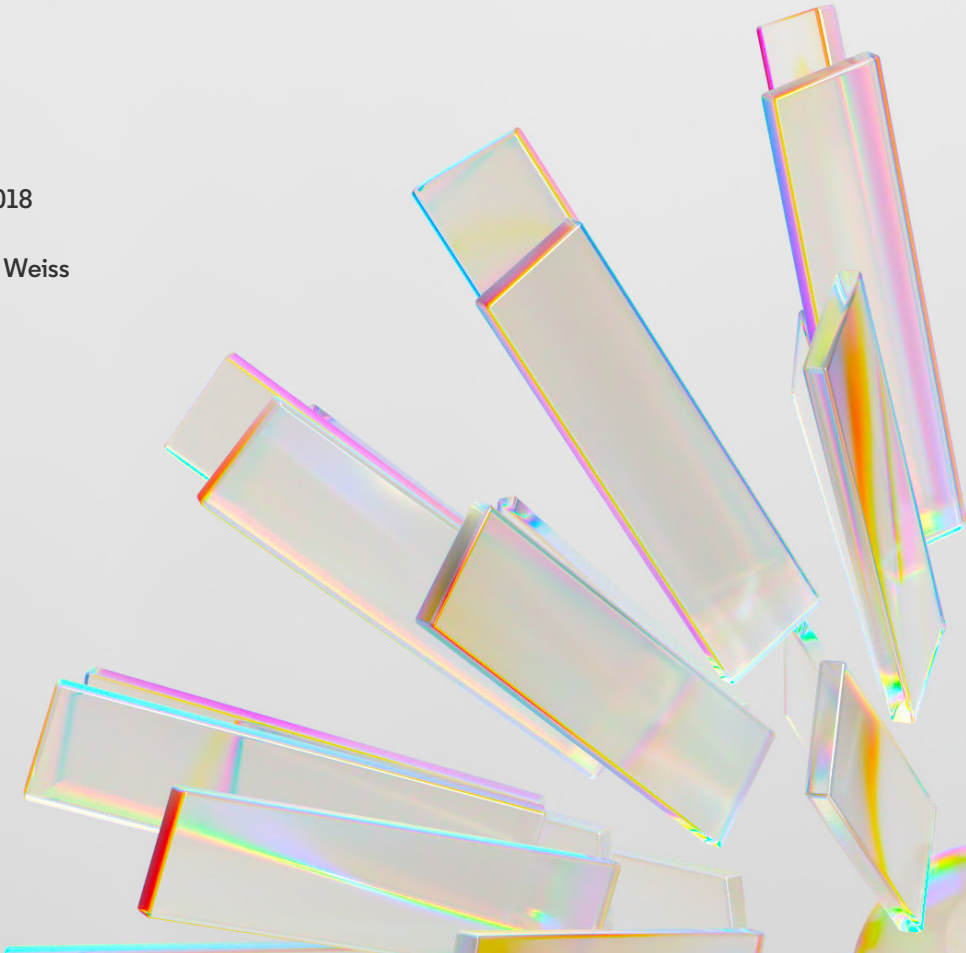
Founded: **2009 (as Kura Therapeutics), launched as Nurix Inc in 2014, became Nurix Therapeutics Inc in 2018**

Founders: **John Kuriyan, Michael Rapé, Arthur Weiss**

Headquarters: **Brisbane, California**

Investors

- N/A (public company: Ticker: NRIX)



Partners

Academic

N/A

Corporate

Gilead Sciences
Collaboration agreement to identify multiple targeted protein degrader candidates using Nurix Therapeutics Inc's proprietary drug discovery platform.

Sanofi
Collaboration and licensing agreement to develop STAT6 degraders, including the lead program, NX-3911.

Seagen Inc (now Pfizer)
Multi-target collaboration agreement to advance DACs for oncology indications by combining Nurix's DEL-AI platform and portfolio of E3 ligase binders with Pfizer's antibody engineering expertise.

What makes this company stand out?

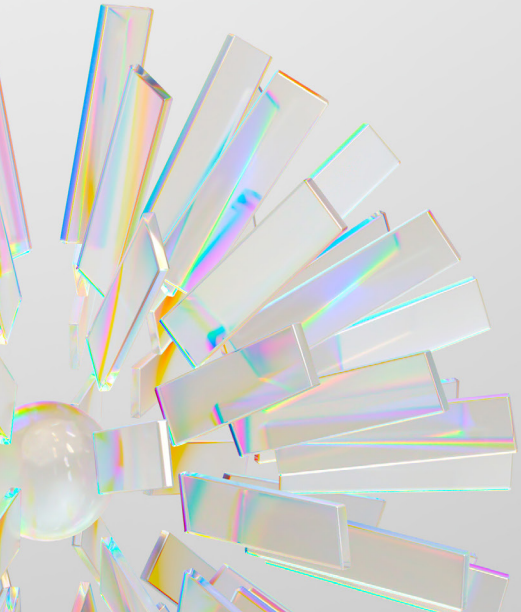
- Nurix Therapeutics was built on pioneering research from UC Berkeley and UCSF that established the structural and biochemical basis for targeted protein degradation. The company's leadership team combines deep scientific expertise with proven drug development and business acumen.
- Nurix has advanced a diversified portfolio of potentially first-in-class therapeutic candidates into the clinic. The company's lead asset NX-5948 (bexobrutideg), the first degrader to carry the "-deg" stem, is demonstrating durable efficacy in B-cell malignancies and is poised for pivotal trials.
- Additional clinical programs include:
  - NX-2127 (zelebrudomide), a dual BTK/IKZF1/3 degrader for aggressive lymphomas.
  - NX-1607, a CBL-B inhibitor for immuno-oncology.
- Strategic collaborations with Gilead (IRAK4 degraders), Sanofi (STAT6 degraders) and Pfizer (DACs) extend Nurix's reach into autoimmune, inflammatory and antibody-based therapeutics. These partnerships help validate the company's platform, bring in non-dilutive capital and create opportunities for shared development and commercialization.
- Nurix's DEL-AI engine integrates DNA-encoded libraries (>5bn compounds), proprietary E3 ligase binders, automated chemistry and ML models trained on proprietary data. This platform has enabled the company to access more than 90 E3 ligases, including many previously considered undruggable, and has accelerated its discovery of wholly owned and partnered clinical candidates.

How will the company's solution benefit patients and their caregivers?

- By harnessing its DEL-AI platform and deep expertise in E3 ligases, Nurix can design medicines that eliminate disease-causing proteins previously considered "undruggable" and could help to transform treatment options for patients with diseases or conditions that currently have few or no effective therapies.
- For patients, this could mean more effective therapies, access to new treatments and improved quality of life.
    - Programs like NX-5948 and NX-2127 provide hope for patients with advanced B-cell malignancies who have exhausted standard-of-care options, while partnered IRAK4 and STAT6 degraders may open new therapeutic paths in autoimmune and inflammatory diseases.
    - Oral, brain-penetrant small molecules such as NX-5948 aim to reduce the burden of hospital-based treatments, giving patients and caregivers more flexibility and less disruption to daily life.
    - The company's wholly owned pipeline, coupled with its partnered programs with Gilead, Sanofi and Pfizer, extends the impact across oncology, immunology and inflammation — areas where unmet need remains high.
- For caregivers, these advances could translate into more time, fewer treatment complications and renewed hope, as Nurix aims for its therapies to not only extend survival but also improve the day-to-day experience of patients and their families.

Funding and grants

- Non-disclosed

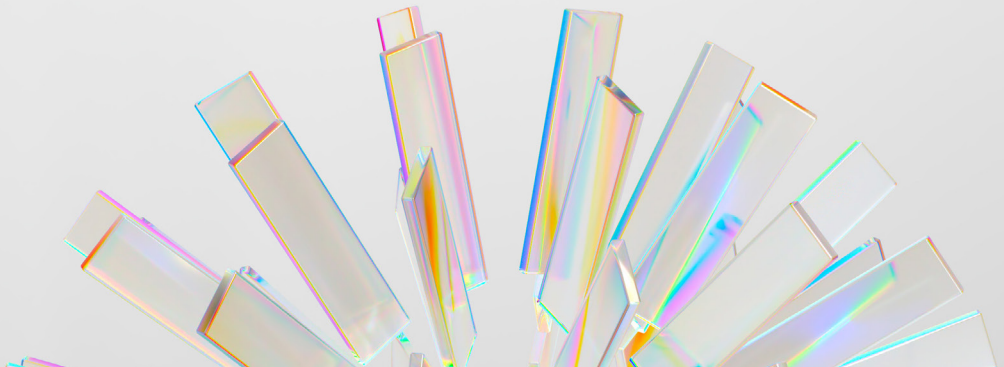


IP status and patent filings

- Nurix maintains a broad and growing intellectual property estate to protect its platform technologies, degrader molecules and therapeutic programs.

R&D activity

- Bexobrutideg (NX-5948), an oral, brain-penetrant BTK degrader being developed for B-cell malignancies, including CLL, SLL and WM, is currently in phase 1b/2 and expected to enter pivotal studies in the second half of 2025.
  - Regulatory designations include:
    - U.S. FDA fast track designation (CLL/SLL, WM)
    - EMA PRIME designation (CLL/SLL)
    - U.S. FDA orphan drug designation (WM)
    - EMA orphan drug designation (lymphoplasmacytic lymphoma)
  - In relapsed/refractory CLL, phase 1 data demonstrated robust responses across all dose levels, independent of prior treatment, baseline mutations or CNS involvement.
- Zelebrudomide (NX-2127), a PROTAC targeting BTK and IKZF1/3 for B cell malignancies with a focus on aggressive forms of NHL, including relapsed/refractory CLL, is in phase 1. Early data demonstrated its ability to result in sustained BTK degradation and clinically meaningful responses independent of prior treatments or BTK mutational status.
- NX-1607, a small molecule inhibitor of CBL-B, is in an ongoing phase 1 dose-escalation trial for advanced solid tumors and lymphomas. The study includes both monotherapy and combination arms (with paclitaxel). Early clinical data confirmed target engagement of CBL-B and support continued development in immuno-oncology.
- NX-0479/GS-6791 (oral IRAK4 degrader) is being co-developed with Gilead Sciences and is designed to treat chronic inflammatory diseases, with an initial focus on rheumatoid arthritis. Following FDA IND clearance in April 2025, Gilead has initiated a phase 1 SAD/MAD trial with healthy volunteers to assess safety, tolerability and pharmacokinetics.
- NX-3911 (STAT6 degrader) is being advanced under a collaboration with Sanofi. NX-3911 targets allergic, autoimmune and inflammatory processes. The program is in IND-enabling studies, with candidate nomination anticipated in 2025.



"At Nurix, we are pioneering a new class of medicines based on targeted protein degradation, with the potential to address diseases that have long resisted traditional approaches. With a strong wholly owned pipeline, productive partnerships, and a discovery engine capable of drugging the undruggable, we are positioned to deliver meaningful new treatments for patients while shaping the future of medicine."

Arthur T. Sands,
MD, PhD, Nurix Therapeutics President and CEO

TRIANA Biomedicines

TRIANA Biomedicines is a private biotechnology company focused on building a leading molecular glue discovery platform to regulate disease targets that are difficult to address with any other modality. TRIANA's drug discovery engine is powered by bespoke chemical libraries and deep biochemical and biological mechanistic insights in addition to high-resolution structural biology. The company's platform enables evaluation and prioritization of over 600 E3 ubiquitin ligases and their disease-relevant targets.

Company profile

Founded: **Launched in 2022**

Founders: **N/A**

Headquarters: **Lexington, Massachusetts**

Investors

- Atlas Venture
- Lightspeed Venture Partners
- Logos Capital
- Pfizer Ventures
- RA Capital Management
- Surveyor Capital (a Citadel company)

Partners

Academic	Corporate
N/A	**Pfizer Inc** Strategic collaboration and licensing agreement to discover and develop novel molecular glue degraders across multiple therapeutic areas.

What makes this company stand out?

- TRIANA's target-first and proximity-first approach to molecular glue discovery is currently focused on inducing or enhancing the degradation of high-profile disease targets. With its therapeutic approach, TRIANA aims to fundamentally change the paradigm of small molecule drug discovery and bring significant therapeutic benefits to patients.
- TRIANA's molecular glue platform is based on a combination of AI algorithms and deep experimental biology know-how. It is used to identify molecular glues that enhance protein-protein interactions, particularly of disease targets with ubiquitin ligases (E3 ligases).
- The company uses a target-first approach leveraging genomic, functional and translational data to prioritize disease targets and candidate E3 ligases for molecular glue discovery.
- Based on a rational, prospective approach, TRIANA uses its proprietary protein:protein pairing engine to identify the preferred E3 ligases for a specific disease target and discover small molecules that directly promote the interaction of the disease target-E3 ligase pair. The multilayered approach involves AI as well as experimental approaches for E3 ligase prioritization.

How will the company's solution benefit patients and their caregivers?

- TRIANA Biomedicines' approach focuses on challenging disease targets responsible for the pathophysiology of specific diseases for which there is a high unmet medical need.

Funding and grants

April 2022: Seed and Series A funding ($110m), co-led by Lightspeed Venture Partners, RA Capital Management and Atlas Venture, with participation from Pfizer Ventures, Surveyor Capital (a Citadel company) and Logos Capital.

IP status and patent filings

- Patents covering novel compounds and methods of inducing degradation of a protein held in multiple countries.

R&D activity

- N/A

"One of TRIANA's strengths lies in our molecular glue and E3-ligase pairing platform, which unlocks the ability to drug difficult targets and enables the creation of transformative medicines that have the potential to bring meaningful benefit to patients. Our target-first approach had us focus our research efforts exclusively on high value oncology targets, which has resulted in an exciting product pipeline with several first-in-class molecular glue degrader opportunities."

Patrick Trojer,
PhD, TRIANA Biomedicines President and CEO

TRIMTECH Therapeutics

Leveraging its academic co-founders' 20 years of research into the biology of TRIM21, an E3 ubiquitin ligase, TRIMTECH Therapeutics aims to address neurodegenerative (e.g., Alzheimer's disease, Huntington's disease) and inflammatory diseases with significant unmet medical need. The company is developing proprietary TRIMTAC® and TRIMGLUE® small molecule degraders designed to recruit TRIM21 for aggregate-selective degradation via the ubiquitin-proteasome system.

Company profile

Founded: **2025**

Founders: **Cambridge Innovation Capital (CIC) and SV Health Investors' Dementia Discovery Fund (DDF), in collaboration with Damian Crowther, Leo James and Will McEwan**

Headquarters: **Cambridge, UK**

Investors

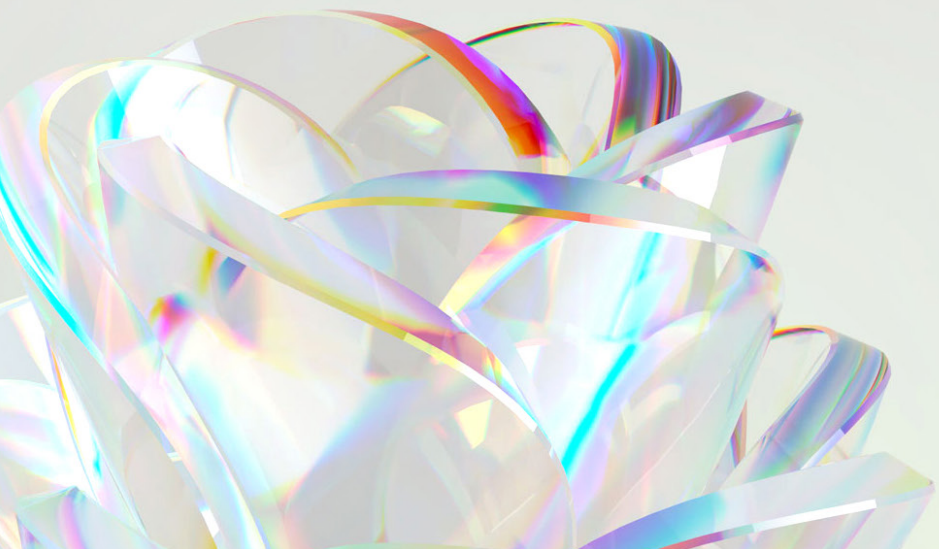
- Cambridge Enterprise Ventures
- CIC
- Eli Lilly and Co
- M Ventures
- MP Healthcare Venture Management (MPH)
- Pfizer Ventures
- Start Codon
- SV Health Investors' DDF

Partners

Academic	Corporate
Non-disclosed	Non-disclosed

What makes this company stand out?

- TRIMTECH Therapeutics' academic co-founders, Leo James (British Medical Research Council [MRC] Laboratory of Molecular Biology) and Will McEwan (U.K. Dementia Research Institute at the University of Cambridge) have pioneered research into the biology of TRIM21, publishing on the topic since 2012.
- The company's portfolio includes therapies that focus on degradation of typically intractable protein aggregates (e.g., tau) or mutant proteins involved in neurodegenerative and inflammatory diseases. TRIM21 enables this while leaving the monomeric forms of the protein required for healthy cellular function untouched.
- The proprietary TRIMTACs are bifunctional molecules leveraging the novel E3 ligase TRIM21 to degrade toxic aggregates implicated in neurodegenerative diseases, while TRIMGLUEs are the equivalent molecular glues.
- Because inbuilt selectivity for aggregate degradation is present with TRIM21, aggregate-selective target binders are not required. This means targets previously out of scope for first-generation degrader approaches can be opened up to targeted protein degradation.



How will the company's solution benefit patients and their caregivers?

- The company is developing small molecule therapies to address the medical needs of large patient populations such as those with Alzheimer's disease who currently have limited treatment options.

Funding and grants

March 2025: Seed funding ($31m), led by CIC and SV Health Investors' DDF, with participation from M Ventures and Pfizer Ventures.

IP status and patent filings

- Non-disclosed

R&D activity

- The company's portfolio focuses on neurodegenerative and inflammatory diseases.

"Through a deep understanding of the function of the novel E3 ligase, we have identified a degrader mechanism that is uniquely suited to selectively degrading intractable toxic aggregate protein targets that underpin a host of severe neurodegenerative diseases. This capability brings us closer to bringing life-changing small molecule degrader treatments that have been out of reach to first generation degrader approaches."

Nicola Thompson,
TRIMTECH Therapeutics CEO

Key takeaways

The recent surge of clinical research and deal-making in the field of targeted protein degraders reflects a growing recognition of their potential to transform treatment approaches for cancers once deemed undruggable, along with other difficult-to-treat diseases. Strategic collaborations and timely acquisitions will be essential to advancing this technology, paving the way for both patient benefit and commercial success.

Targeted protein degrader companies must set themselves apart from others in an increasingly crowded market. To capture the attention of investors and partners, degrader companies will need to demonstrate the unique impact of their platform and/or assets on the therapeutic and competitive landscape.

Life science companies need to perform due diligence when evaluating assets. Awareness of the strengths and limitations of potential partners' platforms, differentiating characteristics and early preclinical data is essential to gain confidence that the platform and/or asset can pass regulatory scrutiny and be accepted by patients and physicians in the market.

Regulatory uncertainty may delay the commercialization of targeted protein degraders. Given the lack of precedent for approvals in this emerging modality, proactive regulatory planning, including early engagement with agencies to address novel mechanism-of-action considerations, biomarkers and trial design requirements, could help improve the likelihood of success.

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