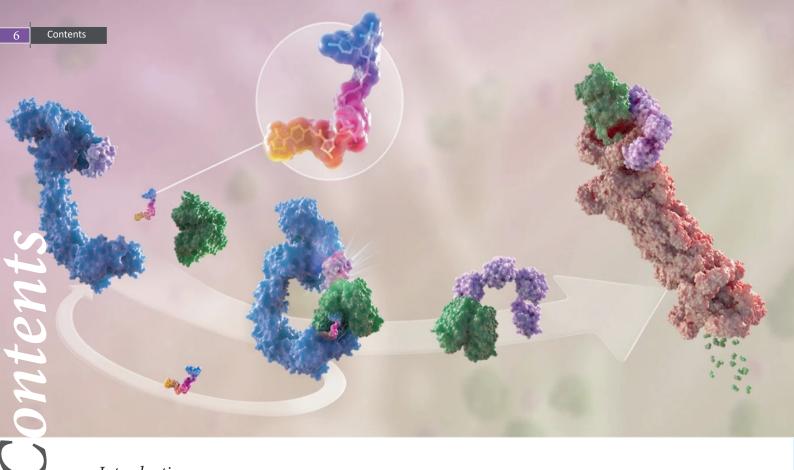


Global Targeted Protein Degraders 2025

Covers 330 Drug Developers with Strategic Insights © Technologies © Patents © Pipeline © Funding © Deals

World's Largest Coverage - GUARANTEED



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Targeted Protein Degradation (TPD) Targets in Development Landscape - 2025

Insights on Emerging Targets Diversity in TPD Space

The TPD landscape is rapidly expanding, with diverse molecular targets spanning oncogenic drivers, epigenetic regulators, apoptosis modulators, immune regulators and neurodegenerative disease markers. This report categorizes these targets into eight key clusters, each representing a distinct therapeutic focus area.

Cluster 1 - Oncogenic Signaling and Kinases -

Intelligence Snapshot with Companies, Molecules, Targets & Current Development Status).

- 1.1 *Growth Factor Receptors* : EGFR (including resistant mutants like C797S), HER2, FGFR3 and c-MET.
- 1.2 Oncogenic Kinases : BRAF (V660X), KRAS (G12C/D), NRas, BTK, CK1α, FLT3, ERK5, Mnk1/2, BCR-ABL and ALK.
- 1.3 *Cell Cycle Regulators* : CDK4/6, CDK7/9, Cyclin D1, Cyclin K, PLK1, WEE1 and CCNK x CDK12.
- 1.4 *Signaling Pathway Kinases*: ATR, AXL, ALK, RAF1, MEK-RAF, PI3K alpha, ILK and TrkA.
- 1.5 *Immune Signaling Modulators:* IRAK-M, FAK, STAT3, PKC-θ, SHP2, Grk2, IL-4Rα and TRIB1.
- 1.6 Hormone Receptors in Cancer : Androgen Receptor (AR) & Estrogen Receptor (ER).

Cluster 2 - Epigenetic and Transcriptional Regulators -

Intelligence Snapshot with *Companies*, *Molecules*, *Targets & Current Development Status*).

- 2.1 *Histone Modifiers & Chromatin Remodelers* : EZH2, KAT2B (PCAF/GCN5), NSD2, PRC2, SMARCA2.
- 2.2 *Transcriptional Regulators & Oncogenic Factors*: IKZF1 (Ikaros), IKZF3 (Aiolos), c-Myc, CBP, EP300/p300, SOX2, MYB, IRF4, Wiz, ZBTB7A, SREBP1 and YAP-TEAD.
- 2.3 BET Proteins : pan-BET, BRD4 and BRD9.
- 2.4 RNA & Protein Translation Regulators : eIF4E, ERG, LSD1, RBM39.

Cluster 3 Apoptosis and Protein Stability Regulators -

Intelligence Snapshot with Companies, Molecules, Targets & Current Development Status).

- 3.1 BCL Family Proteins : BCL-XL, BCL6, BCL-2, MCL-1
- 3.2 MDM2-p53 Axis Restoring Tumor Suppression : MDM2, p53, TP53
- 3.3 Ubiquitin Pathway Regulators : FBXW7, RNF31, UBE2K, USP1, USP7, USP30.
- 3.4 DNA Repair & Genome Stability Regulators : PARP1, Rad51, POLQ, WRN.
- 3.5 GSPT1 Degradation Inducing Apoptosis Through Translation Disruption : GSPT1

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| | 8.3 Fibrosis & Metabolic Regulators (Potential for Fibrotic & Metabolic Disease) : HSP47, ILK | |
| | 8.4 <i>Transcriptional & Epigenetic Regulators:</i> MLLT1/MLLT3 (Transcriptional CoRegulators) ZBTB7A (Pokemon Protein), ARID1B, DNMT1. | |
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| Targeted | Protein | Degradation | (TPD) |
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Section **B**

Individual Profiles of 330 Active Targeted Protein Degrader Drug Developer Companies

Individual Drug Developer Profile includes:

Company Overview

Key Technology Platform Key TPD Linked Patents TPD centered Collaborations, Deals & Partnership. Funding Details

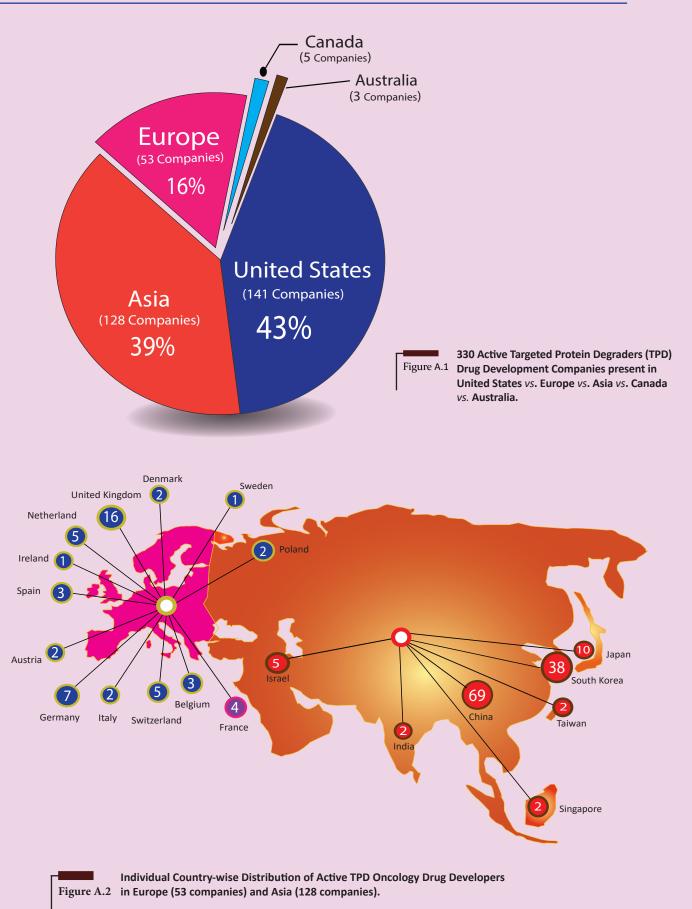
Targeted Protein Degrader Drug Pipeline –Drugs name, its targets, with details of its development for various indications, NCT Number, Degrader Modality.

Management Profile –Address, Contact number, e-mail, Key Management / Decision Maker (CXOs) name and designation, with individual Linked ID and contact emails.

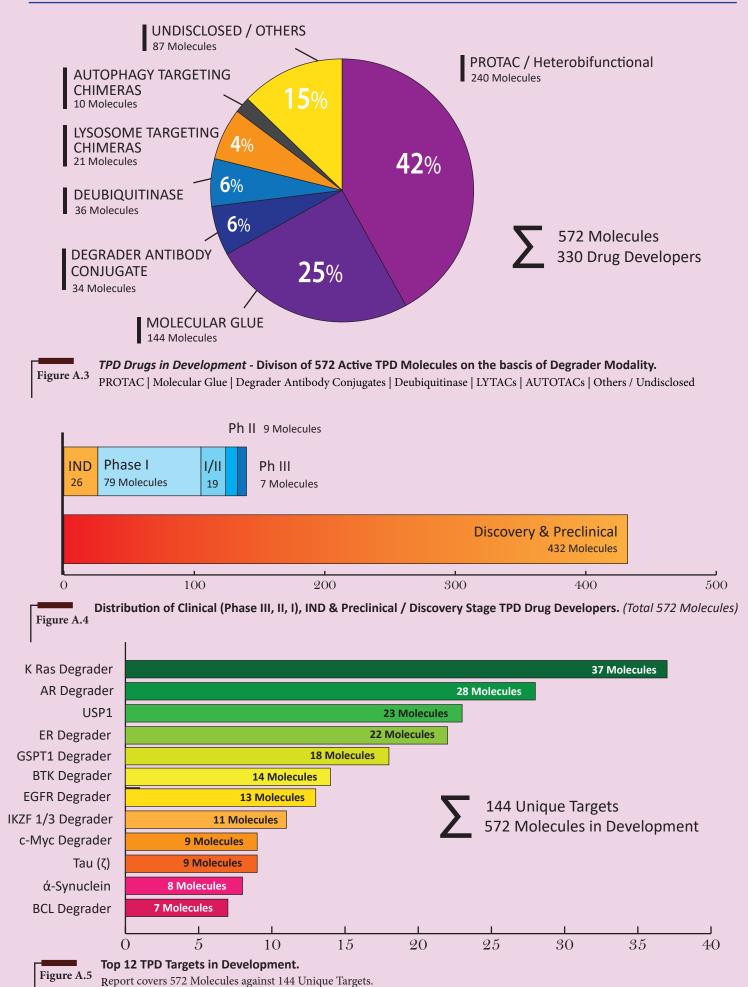
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| EUROPE | Companies Present in Austria |
| | Companies Present in Belgium |
| | Companies Present in Denmark |
| | Companies Present in France |
| | Companies Present in Germany |
| | Companies Present in Ireland |
| | Companies Present in Italy |
| | Companies Present in Netherlands |
| | Companies Present in Portugal |
| | Companies Present in Spain |
| | Companies Present in Sweden |
| | Companies Present in Switzerland |
| | Companies Present in United Kingdom |
| North America | Companies Present in Canada |
| | Companies Present in United States of America |
| A USTRALIA | Companies Present in Australia |

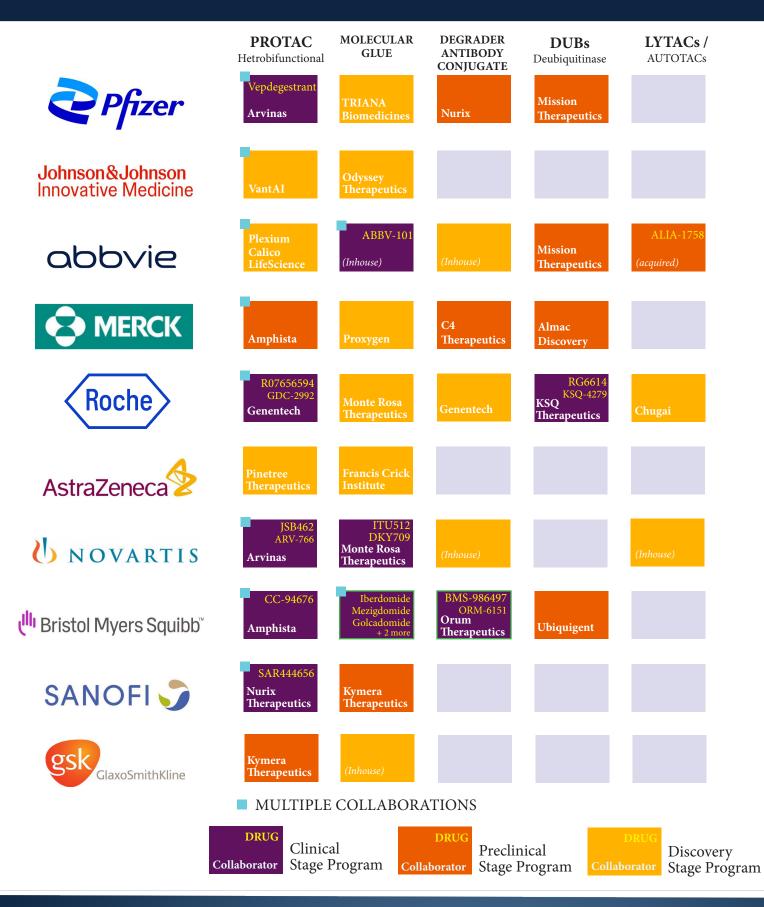
TARGETED PROTEIN DEGRADERS - GLOBAL DISTRIBUTION



TARGETED PROTEIN DEGRADERS - MOLECULES IN DEVELOPMENT



TARGETED PROTEIN DEGRADATION - 2025 TOP 10 PHARMACEUTICALS - ASSETS & COLLABORATIONS



As of Jan 2025, the top 10 pharmaceutical companies were developing 36 TPD molecules. In total, 572 TPD molecules are in active development, including 114 in clinical stages, 26 in IND stages, and 432 in preclinical stages.

330 Targeted Protein Degraders Intelligence Snapshot

TARGETED PROTEIN DEGRADATION (TPD) DRUG DEVELOPER'S KEY PATENTS - 2025

Drug Developer's TPD Linked Patent Details (184 Companies | 337 Patents) Table No. A.7

| No. | COMPANY NAME | Key TPD Linked Patents (title) | PATENT NUMBER | DATE |
|-----|-------------------------------|--|-----------------|----------|
| 1. | 76Bio, Inc. | Developing dual-specific bifunctional polypeptides that induce degradation of a biological target through the cel- lular proteasome mechanism. | WO2024081913A1 | Oct-23 |
| | | Bifunctional fusion proteins for ubiquitin-mediated degradation. | WO2023215839A1 | May-23 |
| 2. | Accutar Biotechnology, Inc | ccutar Biotechnology, Inc Glutarimide-containing pan-KRAS-mutant degrader compounds and uses thereof | | Nov-2022 |
| | | Heterocyclic compounds as e3 ligase inhibitors | WO2024073502A1 | Sep-2022 |
| 3. | Adlai Nortye Limited | Cyclin k degradation agent. | WO2023025225A1 | Aug-22 |
| | | Novel pomalidomide derivatives and preparation method therefor | WO2023249470A1 | Jun-23 |
| 4. | AevisBio, Inc. | Specific Compound Binding for Target Protein and Tar- get Degrader, Pharmaceutical Compositions Comprising the Same, and the Use thereof | KR20240141067A | Mar-23 |
| 5. | Almac Discovery Ltd. | Piperidine derivatives as inhibitors of ubiquitin specific protease 7. | AU2017346516B2 | Oct-2016 |
| Ј, | Annae Discovery Ltd. | Heterocyclic compounds as ubiquitin specific protease 7 inhibitors. | WO2023139241A1 | Jan-2022 |
| 6. | Amphista Therapeutics | Targeted protein degradation of KRAS(G12D). | GB202208860D0 | Jun-2022 |
| 0. | Limited | Targeted protein degradation of EGFR | GB202208888D0 | Jun-2022 |
| 7. | Angiex, Inc. | Degrader-antibody conjugates and methods of using same. | WO2021195598A2 | Mar-2021 |
| 8. | AnHorn Medicines Co., Ltd. | Bifunctional compound and pharmaceutical composition | WO2024002206A1 | Jun-2022 |
| | Amouton | Small molecule compounds | US20240350463A1 | Jun-2022 |
| 9. | i marmace acreato, me. | Disclosed herein are pharmaceutical compositions com- prising biosynthetic allosteric mTOR inhibitors | US20230104503A1 | Jun-2021 |
| 10. | | Compounds for degrading tau protein aggregates and uses thereof | WO2021097243A1 | Nov-2020 |
| 10. | Aprinoia Therapeutics, Inc. | Compounds for degrading α -synuclein aggregates and uses thereof | US11291732B1 | May-2021 |
| 11. | Aptadegrad S.L. | Dna aptamer conjugates recognizing and degrading coro- navirus proteins | WO2024003300A1 | Jun-23 |
| 12. | Arrakis Therapeutics, Inc. | RNA degraders and uses thereof | WO2024112918A1 | Nov-2022 |
| 12 | Aminos Inc | Indazole based compounds and associated methods of use. | US20240360152A1 | May-2024 |
| 13. | Arvinas, Inc. | Use of an Androgen Receptor degrader PROTAC for the treatment of prostate | WO2024220926A1 | Apr-2023 |

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TARGETED PROTEIN DEGRADATION (TPD) CLINICAL & IND STAGE PIPELINE COVERAGE - 2025

Clinical-Stage Targeted Protein Degraders (TPDs) Molecules in Development (81 Companies Developing 110 Molecules)

Table No. A.8

| No. | COMPANY NAME | COUNTRY | MOLECULE NAME | TARGET | PHASE | INDICATION | NCT NUMBER | DEGRADER MODALITY | | |
|-----|---------------------------------------|---------------------------|-----------------------------|---------------------------------|----------------------|--|---------------------|---------------------------------|--------------------------------|--------------------------------|
| 1. | Bristol Myers | United | Mezigdomide / CC-92480 | IKZF1/3 | III | R/R Multiple Myeloma | NCT05552976 | CELMoD (Molecular Glue) | | |
| 1. | Squibb | States | Iberdomide / CC220 | IKZF1/3 | III | Multiple Myeloma | NCT04975997 | CELMoD (Molecular Glue) | | |
| 2. | Pfizer, Inc. | United States | Vepdegestrant / ARV-471 | ER | III | Breast Cancer | NCT05654623 | PROTAC | | |
| 3. | AstraZeneca | United Kingdom | Camizestrant / AZD9833 | ER | III | ER+/HER2- Advanced Breast Cancer | NCT04964934 | SERD | | |
| 4. | Eli Lilly and Company | United States | Imlunestrant / LY3484356 | ER | III | Metastatic Breast Cancer | NCT04975308 | SERD | | |
| 5. | Roche Ltd. | Switzer- land | Giredestrant / GDC-9545 | ER | III | Breast Cancer | NCT06065748 | SERD | | |
| 6. | Eisai Inc | Japan | E7820 | RBM23/39 | II | Acute Myeloid Leukemia | NCT05024994 | Molecular Glue | | |
| 7. | Innovo Therapeutics | United States | INV-001 | HSP47 | II | Scar | NCT05838833 | Targeted Protein Degradation | | |
| 8. | Kintor Phar- maceutical Limited | China | GT20029 | AR | II | Androgenetic Alopecia | NCT06692465 | Heterobifunctional Degrader | | |
| 9. | Kymera Therapeutics | herapeutics United States | KT-474 / (SAR444656) | IRAK4 | II | Atopic Dermatitis | NCT06058156 | Monovalent | | |
| | Inc. | | | (SAR444656) | (SAR444656) | (SAR444656) | (SAR444656) | intinti | II | Hidradenitis Sup- purativa |
| | MISSION | United | MTX652 | USP30 | II | Heart Failure | | DUB | | |
| 10. | Therapeutics | Kingdom | MTX325 | USP30 | II | Parkinson's Dis- ease | IS- RCTN20898392 | DUB | | |
| | | | | | II | Atopic Dermatitis | NCT06058156 | | | |
| 11. | Sanofi SA | France | SAR444656 | IRAK4 | II | Hidradenitis Suppurativa | NCT06028230 | Chimeric Degrader | | |
| 12. | AbbVie Inc. | United States | ABBV-101 | BTK De- grader WT & C481S | Ι | B-Cell Malignancies | NCT05753501 | Molecular Glue | | |
| | | | AC0176 | Androgen Receptor | Ι | Prostate Cancer (mCRPC) | NCT05241613 | Heterobifunctional Degrader | | |
| | Accutar Biotechnology Inc. | United | AC0682 | Estrogen Receptor | Ι | Metastatic ER+ Breast Cancer | NCT05080842 | Heterobifunctional Degrader | | |
| 13. | | 07 | States | AC0699 | Estrogen Receptor | Ι | Breast Cancer | NCT05654532 | Heterobifunctional Degrader | |
| | | | | | AC0676 | BTK De- grader (WT & C481S) | Ι | B-Cell Malignancies | NCT05780034 | Heterobifunctional Degrader |

Targeted Protein Degradation Targets Development Landscape - 2025

Targeted Protein Degradation (TPD) Targets can be Grouped in Eight Major Clusters based on their Function and Disease Indication -

1.1 Oncogenic Signaling and Kinases -

These targets regulate critical pathways involved in cancer progression, proliferation, and survival.

1.2 Epigenetic and Transcriptional Regulators -

Focus on modulating gene expression and chromatin remodeling for various diseases.

1.3 Apoptosis and Protein Stability Regulators -

Key modulators of programmed cell death and protein homeostasis

1.4 Structural and Metabolic Pathway Modulators -

Targets involved in oxidative stress responses, intracellular metabolism and extracellular matrix remodeling.

1.5 <u>Neurodegenerative and Rare Disease Targets</u> -

Proteins implicated in neurodegeneration and rare genetic disorders.

1.6 *Immune Modulation and Inflammatory Disease Targets* - Torrects involved in immune properties and inflammation

Targets involved in immune regulation and inflammation.

1.7 Viral and Pathogen Associated Targets -

Targets to address viral and bacterial infections.

1.8 <u>*Emerging and Miscellaneous Targets*</u> -Unconventional or niche targets expanding the scope of TPD.

CLUSTER 1 : ONCOGENIC SIGNALLING AND KINASES (163 companies)

Key Focus Areas: Growth factor receptors, oncogenic kinases, cell cycle regulators, signaling pathway modulators, and hormone-driven cancer targets.

TPDs are emerging as a breakthrough approach to **overcome therapy resistance** and drive tumor regression in various cancers. This cluster focuses on targets that fuel **oncogenic signaling, regulate cell proliferation and modulate immune escape mechanisms**, offering novel avenues for precision oncology.

Key Target Groups:

- * <u>Cluster 1.1</u> Growth Factor Receptors : EGFR (including resistant mutants like C797S), HER2, FGFR3 and c-MET. (*16 Molecules*)
- * <u>Cluster 1.2</u> Oncogenic Kinases : BRAF (V660X), KRAS (G12C/D), NRas, BTK, CK1α, FLT3, ERK5, Mnk1/2, BCR-ABL and ALK. *(64 Molecules)*
- *Cluster 1.3 Cell Cycle Regulators : CDK4/6, CDK7/9, Cyclin D1, Cyclin K, PLK1, WEE1 and CCNK x CDK12. (27 Molecules)
- * <u>Cluster 1.4</u> Signaling Pathway Kinases: ATR, AXL, ALK, RAF1, MEK-RAF, PI3K alpha, ILK, TrkA. *(16 Molecules)*
- * <u>Cluster 1.5</u> Immune Signaling Modulators: IRAK-M, FAK, STAT3, PKC-θ, SHP2, Grk2, IL-4Rα and TRIB1. *(11 Molecules)*
- <u>Cluster 1.5</u> Hormone Receptors in Cancer Androgen Receptor (AR) : Crucial in prostate cancer progression. Estrogen Receptor (ER) and Selective Estrogen Receptor Degraders (SERDs) : Key regulators in HR+ breast cancer. (54 Molecules)

Market Outlook:

With multiple **TPD-based candidates advancing through clinical trials**, targeting *oncogenic kinases, hormone receptors* and *immune modulators* represents **one of the most dynamic areas** in precision oncology. The **degradation-first** approach is reshaping cancer therapy, addressing resistance mechanisms, and expanding treatment options for hard-to-treat cancers.

CLUSTER 1.1 : Growth Factor Receptors (16 Molecules)

Table No. D.1

TARGETS : EGFR (including C797S-resistant mutants), HER2, FGFR3, C-MET

| No. | Company Name | COUNTRY | Molecule Name | TARGET | Phase | INDICATION | DEGRADER MODALITY |
|-----|---|------------------|----------------------|-------------|-------------|----------------------------------|--|
| 1. | C4 Therapeutics Inc | United States | CFT8919 | EGFR, L858R | Ι | Non Small Cell Lung Cancer | BiDAC |
| 2. | Haisco Pharmaceuti- cal Group Co., Ltd. | China | HSK40118 | EGFR | Ι | Non-small cell lung cancer | Heterobifunctional |
| 3. | Jing Medicine Tech- nology (Shanghai), Ltd. | China | HJ-002-03 | EGFR C797S | Ι | Non-Small Cell Lung Cancer | Heterobifunctional |
| 4. | Betta Pharmaceuti- cals Co., Ltd. | China | CFT8919 | EGFR | IND | Non Small Cell Lung Carcinoma | BiDAC |
| 5. | Epibiologics, Inc. | United States | EPI-326 | EGFR | IND | Non-Small Cell Lung Carcinoma | Degrader Antibody Conjugates (DACs) |
| 6. | GlueTacs Therapeutics | China | GT868 | EGFR | Preclinical | Non-small cell lung cancer | GLUETAC Degrader |
| 7. | Bridge Biotherapeutics, Inc. | South Korea | BBT-176 | EGFR | Preclinical | Oncology | Heterobifunctional |
| 8. | HK inno.N Corporation | South Korea | Undisclosed | EGFR | Preclinical | Oncology | Heterobifunctional |
| 9. | J2H Biotech, Inc. | South Korea | J2H-2002 | EGFR | Preclinical | Non-Small Cell Lung Cancer | Heterobifunctional |
| 10. | Polymed Biopharmaceuticals | China | HPB-001 | EGFR | Preclinical | Neoplasms | Heterobifunctional |
| 11. | TYK Medicine, Inc. | China | TY-3200 | EGFR | Preclinical | Solid Tumors | Heterobifunctional |
| 12. | Orum Therapeutics Inc. | South Korea | ORM-5029 | Her2 | Ι | HER2-positive Breast Cancer | Molecular Glue |
| 13. | Chengdu Fendi Phar- maceuticals Co., Ltd. | China | FD-004 | HER2 | Preclinical | Oncology | Degrader Antibody Conjugates |
| 14. | Blueprint Medicines Corporation | United States | Undisclosed | FGFR3 | Preclinical | Oncology | Heterobifunctional |
| 15. | Pierre Fabre Laboratories | Japan | PFL-002/ VERT-002 | c-MET | I/II | Non-Small Cell Lung Cancer | Degrader Antibody Conjugates |
| 16. | Oncozen Co., LTD. | South Korea | OZ-003 | cMET | Discovery | Non Small Cell Lung Cancer | Heterobifunctional |

TARGETED PROTEIN DEGRADATION (TPD) FUNDING & DEALS LANDSCAPE - 2025

Targeted Protein Degradation Drug Development Companies -Private Financing 2023 - 2024

Table No. A.13

| No. | Company Name | COUNTRY | Funding Amount | Funding Round | Month / YEAR | Key Investors in the Round |
|-----|---|------------------|------------------------------------|------------------|-----------------|---|
| 1. | 76Bio, Inc. | United States | \$12.2 Mn | Undisclosed | Feb-23 | Two River Group Holdings |
| | | TT : 1 | \$14.5 Mn | Grant | May-24 | Department of Defense |
| 2. | A-Alpha Bio, Inc. | United States | \$22.4 Mn | Series A2 | Jul-23 | Xontogeny Ventures, Madrona |
| 3. | AevisBio, Inc. | South Korea | 600 Mn KRW | Grant | Jan-23 | National Research Foundation of Korea |
| 4. | AIGEN Sciences Inc. | South Korea | 12 billion KRW (US \$8.8 Mn) | Series A | Oct-24 | Quad Investment Management. Medytox Venture Investment, Premier Partners, K2 Investment Partners, Scale Up Partners |
| 5. | AnHorn Medicines Co., Ltd. | Taiwan | \$10 Mn | Series A | Apr-23 | TaiAn Technologies, Industrial Technology Investment Corporation, Hong Tai Electric Industrial, Black Marble Capital Management, Mega Venture Capital and Sunplus Technology. |
| 6. | Aurigene Oncology Limited | India | ₹6,500 Mn | Undisclosed | May-24 | Dr. Reddy's Laboratories |
| 7. | Automera Pte. Ltd | Singapore | \$16 Mn | Series A | Sep-23 | ALSP and ClavystBio, EDBI, Xora Innovation |
| 8. | Avilar Therapeutics, Inc. | United States | \$75 Mn | Seed | Feb-23 | RA Capital Management, Sanofi Ventures, Medical Excellence Capital (MEC), Astellas Venture Management (AVM). |
| 9. | Biolexis Therapeutics, Inc. | United States | \$10 Mn | Series A | Nov-23 | Clarke Capital |
| 10 | Chengdu Zeling Biomedical Tech- nology Co. Ltd. | China | 106.5 Mn Yuan | Series B | Nov-23 | Precision Medicine Industry Innovation Fund (man- aged by Chengdu Science and Technology Venture Capital) and Huajin Capital, Ceyuan Capital, Shengzhong Investment. |
| 11. | ChomiX Biotech Co., Ltd. | China | N/A | Pre A Series | May-23 | TigerYeah Capital Tsinghua Innovation Ventures Morning Spring Venture. |
| 12 | ConfometRx, Inc. | United States | N/A | Grant | Sep-23 | SBIR |
| 12. | | | N/A | Grant | Jul-23 | SBIR |
| 13. | Cullgen, Inc. | United States | \$35Mn | Series C | May-23 | AstraZeneca-CICC Venture Capital Partnership, Sincere Capital, Voyagers Capital, Wuxi Capital Group and GNI Group Ltd. |
| 14. | Degrome Therapeutics, Inc. | United States | \$0.5 Mn | Grant | Sep-24 | National Institute on Aging |
| 15. | Degron Therapeutics, Inc. | China | \$34.5 Mn | | Dec-24 | Undisclosed |

Targeted Protein Degradation Drug Development Companies Research Collaboration with Non Profit Organizations (19 Deals)

| No. | Early Stage Onco Drug Developer | Partner Company | Month | DESCRIPTION |
|-----|---|---|--------|---|
| 1. | BPGbio, Inc. | University of Oxford | Oct-24 | BPGbio and University of Oxford enter into strategic collaboration focused on breakthrough E2- based Protein Degradation research in Oncology and CNS diseases. |
| 2. | Livzon Pharmaceutical Group, Inc. | Shanghai Institute of Organic Chemistry and the University of Michigan | Sep-24 | Scientists at Livzon Pharmaceutical Group Inc., Shanghai Institute of Organic Chemistry and the University of Michigan have identified proteolysis targeting chimeras (PROTACs) comprising an E3 ubiqui- tin ligase binding moiety covalently bound to a cyclin-dependent ki- nase 12 (CDK12) and 13 (CDK13) targeting moiety through a linker reported to be useful for the treatment of cancer. |
| 3. | Livzon Pharmaceutical Group, Inc. | State Key Laboratory of Chemical Biology and International Cooperative Labora- tory of Traditional Chinese Medicine | Dec-23 | Livzon Pharmaceutical collaborated with State Key Laboratory of Chemical Biology and International Cooperative Laboratory of Traditional Chinese Medicine Modernization and Innovative Drug Discovery of Chinese Ministry of Education (MOE) have discovered LHF418 as a new potent SOS1 PROTAC degrader. |
| 4. | Beactica AB | National Center for Advancing Trans- lational Sciences (NCATS) | Sep-23 | Beactica Therapeutics signed research collaboration with the National Center for Advancing Translational Sciences (NCATS), to evaluate Beactica's proprietary targeted TEAD degraders efficacy in disease- relevant preclinical models. NCATS to also map systematically the drug-combination landscape for selected preclinical candidates by performing a highthroughput drug-combination screen. |
| 5. | Astrazeneca Plc | Francis Crick Insti- tute and Imperial College London | May-23 | AstraZeneca partnered with the Francis Crick Institute and Imperial College London to advance the discovery of new molecular glues aimed at treating a range of diseases. This partnership recieved nearly £22.5 Mn in funding through Prosperity Partnership grant from the Engineering and Physical Sciences Research Council (EPSRC) and from AstraZeneca. |
| 6. | Genoscience Pharma | Yissum Research De- velopment Company of the Hebrew Uni- versity of Jerusalem Ltd. | Apr-23 | Genoscience Pharma sign a new research agreement with Yissum Re- search Development Company of the Hebrew University of Jerusalem Ltd., the wholly owned subsidiary and technology transfer company of the Hebrew University of Jerusalem. The collaboration aims to expand the development of PROTAC technology on investigative Genoscience agents, which can increase the potency and selectivity of small molecule drugs and overcome cancer resistance to existing therapies. |
| 7. | Nexo Therapeutics, Inc. | MD Anderson | Jul-23 | MD Anderson and Nexo Therapeutics signed strategic research col- laboration to work together from discovery through investigational new drug-enabling studies to accelerate development of small-mole- cule therapies for patients with limited treatment options. |
| 8. | Manhattan Biosolutions LLC | Wisconsin Alumni Research Foundation (WARF) | May-23 | Manhattan BioSolutions entered into an exclusive option agreement with the Wisconsin Alumni Research Foundation (WARF) for the in- novative pan-RNA degrader technologies (pRNAD) in oncology. |
| 9. | Livzon Pharmaceutical Group, Inc. | International Coop- erative Laboratory of Traditional Chinese Medicine Moderni- zation and the State Key Laboratory of Bioorganic & Natural Products | Feb-23 | Livzon Pharmaceutical collaborated with the International Coopera- tive Laboratory of Traditional Chinese Medicine Modernization and the State Key Laboratory of Bioorganic & Natural Products Chemistry to advance the discovery of AXL degraders with Improved Potencies in Triple-Negative Breast Cancer. |
| 10. | Bridge Biotherapeutics, Inc. | Scripps Research | Aug-22 | Biotherapeutics and Scripps Research launch research collaboration in the fields of covalent targeting and chemical biology. The com- pany aims to develop novel therapeutics for high-value targets in the oncology and immunology space and believes that innovative reactive group chemistries combined with proteomics can facilitate this objec- tive. Bridge seeks to discover proprietary, tunable ligands for covalent drug development and protein degrader applications. |

330 T<u>ARGETED PROTEIN DEGRADERS</u> PROFILES

AbbVie, Inc.

1 North Waukegan Roadwww.abbvie.comFounded: 2013North Chicago, IL 60064,-Employee: 10,000+United States+1 847-932-7900Ownership: Public

HIGHLIGHTS

- ★ AbbVie (ABBV : NYSE) is actively engaged in the field of targeted protein degradation (TPD), focusing on developing innovative therapies across various therapeutic areas, including oncology and neuroscience. Their research involves designing protein degraders that bind to specific proteins and trigger their degradation via the proteasomal pathway.
- ★ AbbVie's internal research teams have been exploring Degradomers—molecules that degrade proteins within cells. Their work focuses on building a sustainable and scalable platform for protein degradation across different therapeutic areas, including on-cology, immunology, and neurology.
- * Key Patents 1. ANTI-HUMAN CD33 BET DEGRADER ANTIBODY-DRUG CONJUGATES. US20250000993A1 (Jan 2025).
- * Pyrimidines for degrading Bruton's tyrosine kinase US12172992B2 (Dec 2024)
- ★ TPD Linked Deals & Collaborations In Oct 2024, AbbVie acquired Aliada Therapeutics for \$1.4 billion, aiming to bolster its Alzheimer's treatment portfolio. This acquisition focuses on Aliada's experimental antibody therapy, ALIA-1758, designed to degrade amyloid beta plaques in the brain, highlighting AbbVie's commitment to advancing TPD in neurological conditions.
- ★ In Aug 2022, Plexium and AbbVie entered into an exclusive strategic collaboration to develop and commercialize novel Targeted Protein Degradation (TPD) therapeutics for neurological conditions. Under the terms, Plexium will run preclinical research for the companies' targets. Once completed, AbbVie will have the option to pick programs for more research and development. Further financial details remains undisclosed.
- ★ In Dec 2020, Frontier Medicines Corporation and AbbVie signed multi-year collaboration to utilize Frontier's proprietary chemoproteomics platform to identify small molecules for programs directed to novel E3 ligases and certain oncology and immunology targets. Under the terms, Frontier received \$55 Mn as an upfront and is eligible to receive additional milestone payments. In addition, AbbVie will reimburse Frontier's R&D costs through defined stages of pre-clinical development. AbbVie will assume full responsibility for global development and commercialization activities and costs for the programs. Frontier will be eligible to receive milestone payments that could potentially exceed \$1 billion, in addition to royalty payments on commercialized products.
- ★ In Nov 2018, Mission Therapeutics and AbbVie signed collaboration to develop DUBs molecules targeting Alzheimer's and Parkinson's Disease. No financial details have been disclosed. The collaboration does not include any of Mission's lead DUB programs including USP30 and USP10.
- ★ AbbVie Calico Life Sciences (an Alphabet Company) Collaboration -:- In 2014, AbbVie and sign Calico Life Science, signs multi year collaboration to discover, develop and bring to market new therapies for patients with age-related diseases, including neurodegeneration and cancer. Under this collaboration, the two companies produced more than two dozen early-stage programs addressing disease states across oncology and neuroscience.
- ★ In 2018, both companies extended their collaboration to reshape their further development responsibilities. Under the terms, Calico will be responsible for research and early development until 2022 and will advance collaboration projects through Phase 2a through 2027. AbbVie will continue to support Calico in its early R&D efforts and, following completion of Phase 2a studies, will have the option to manage late-stage development and commercial activities. Both parties will share costs and profits equally. AbbVie and Calico will each commit to contribute an additional \$500 Mn to the collaboration.
- ★ As a part of this collaboration, Abbvie Inc. and Calico Life Sciences LLC has led to the development of proteolysis targeting chimera (PROTAC) compounds comprising an E3 ubiquitin ligase binding moiety covalently linked to tyrosine-protein phosphatase nonreceptor type 2 (PTPN2; TCPTP) and/or PTPN1B. They are reported to be useful for the treatment of cancer, type 2 diabetes and nonalcoholic steatohepatitis (NASH).
- ★ Abbvie is in research collaboration with Germany based PROXIDRUGS, which has developed a versatile assay, screening and molecular profiling platforms for the identification and characterisation proximity-inducing molecules, with a particular focus on molecular glues for the treatment of neurological diseases, cancer and other disorders.

TARGED PROTEIN DREGRADER PIPELINE

| Name | Target | Phase | Indication | NCT Number | Degrader Modality |
|-----------|--------------|-------------|----------------------|-------------|-------------------|
| ABBV-101 | ВТК | I | B-cell Malignancies | NCT05753501 | Molecular Glue |
| ALIA-1758 | Amyloid beta | Preclinical | Alzheimer's Diseases | | LYTAC |

TARGED PROTEIN DREGRADER PIPELINE (In Collaboration)

| Partner | Program | Target | Phase | Indication | NCT Number | Degrader Modality |
|----------------------|----------------|-------------|-------------|----------------------|------------|-------------------|
| Mission Therapeutics | 6 Confidential | Undisclosed | Preclinical | Alzheimer's Diseases | - | DUB |
| Mission Therapeutics | Confidential | Undisclosed | Preclinical | Alzheimer's Diseases | - | DUB |

Drug Descriptions

* ABBV-101: A small molecule degrader targeting Bruton's tyrosine kinase (BTK), currently in Phase 1 clinical trials for the treatment of B-cell malignancies.

- * ALIA-1758: An experimental bispecific antibody therapy designed to degrade amyloid beta plaques in the brain, aimed at treating Alzheimer's disease.
- * ABBV 484 is a small IO molecule, it is being studied in participants with locally advanced or metastatic tumors.
- Calico is responsible for research and early development and will advance collaboration projects into Phase 2a, including ABBV-CLS-579. AbbVie
 will continue to support Calico in its early R&D efforts and, following completion of Phase 2a studies, will have the option to manage late-stage
 development and commercial activities.

CORPORATE PROFILE

Michael E. Severino, Vice Chairman and President

Thomas Spalding, Vice President, Oncology

thomas.spalding@abbvie.com

Linked in profile

Accutar Biotechnology, Inc.

8 Clarke Drive Suite 4, Cranbury, NJ 08512 United States www.accutarbio.com corporate@accutarbio.com +1 929-262-0884 Founded: 2015 Employee: 11-50 Ownership: Private

HIGHLIGHTS

- ★ Accutar Biotechnology, Inc. is a clinical stage biotechnology company focusing on artificial intelligence (AI)-enabled drug discovery to develop orally bioavailable, chimeric degrader molecules targeting cancer.
- ★ Key Technologies -PPI-TAC (Protein-Protein Interaction Targeting Chimera) platforms creates chimeric molecules to precisely target and modulate protein-protein interactions (PPIs), offering a novel approach for diseases like cancer. By bridging or disrupting specific PPIs, these chimeras selectively degrade or alter disease-related proteins, advancing targeted therapies.
- * *Key Patents* 1. Glutarimide-containing pan-KRAS-mutant degrader compounds and uses thereof. US20240294527A1. (Dated : 2022-11-30)
- ★ 2. Heterocyclic compounds as e3 ligase inhibitors. WO2024073502A1. (Dated : 2022-09-28)
- ★ TPD Linked Deals & Collaborations In Nov 2023, Accutar and Evommune, Inc. collaborate for the discovery of inflammatory diseases by leverage Accutar's AI drug discovery platform. The financial details involved were not disclosed.
- Funding In Aug 2021, Accutar Biotech raised undisclosed funds in a new round of funding from Yunfeng Capital, Coatue, and 3W Healthcare Fund. Since inception, Accutar Biotech has raised nearly US\$100 Mn to support the advancement of its artificial intelligence (AI)-empowered platform and the expansion of proprietary drug pipeline.

TARGED PROTEIN DREGRADER PIPELINE

| Name | Target | Phase | Indication | NCT Number | Degrader Modality |
|-------------|--|-------------|------------------------------|-------------|--------------------|
| AC0176 | AR | I | Prostate Cancer (mCRPC) | NCT05241613 | Heterobifunctional |
| AC0682 | ER alpha | I | Metastatic ER+ Breast Cancer | NCT05080842 | Heterobifunctional |
| AC0699 | ER alpha | I | Breast Cancer | NCT05654532 | Heterobifunctional |
| AC0676 | BTK (WT & C481S) | I | B-Cell Malignancies | NCT05780034 | Heterobifunctional |
| Undisclosed | Undisclosed (Multiple Novel E3 Ligases) | Preclinical | Cancer | - | Heterobifunctional |

DRUG DESCRIPTIONS

- * AC0176 is an investigational orally bioavailable, Heterobifunctional (PROTAC) degrader of AR for the potential treatment of prostate cancers.
- * In preclinical studies, AC0176 demonstrated potent and selective AR protein degradation with broad coverage of AR mutants, favorable pharmacological properties, as well as promising anti-tumor activity in animal models.
- * AC0682 is an investigational orally bioavailable, Heterobifunctional (PROTAC) degrader of ERα for the potential treatment of ER-positive breast cancers. ERα is a hormone-regulated transcription factor that plays a critical role in breast cancer initiation and proliferation, and nearly 80% of breast cancers express ERα.
- * AC699 is a potent and selective orally bioavailable, chimeric degrader of estrogen receptor (ER) α, and offers a potential new breast cancer treatment option based on a differentiated mechanism of action as compared to fulvestrant and novel SERDs with deeper ERα degradation.
- * AC0676, an orally bioavailable, chimeric degrader molecule designed to target and degrade Bruton's Tyrosine Kinase (BTK) with high potency, selectivity, and broad mutant coverage.

CORPORATE PROFILE

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