

TROY TECHNICAL

DRUG DISCOVERY & DDS

WEEKLY REPORT

October 17 - October 23, 2026 | Issue 2026-W42

**Target validation, translational evidence,
delivery and development economics**

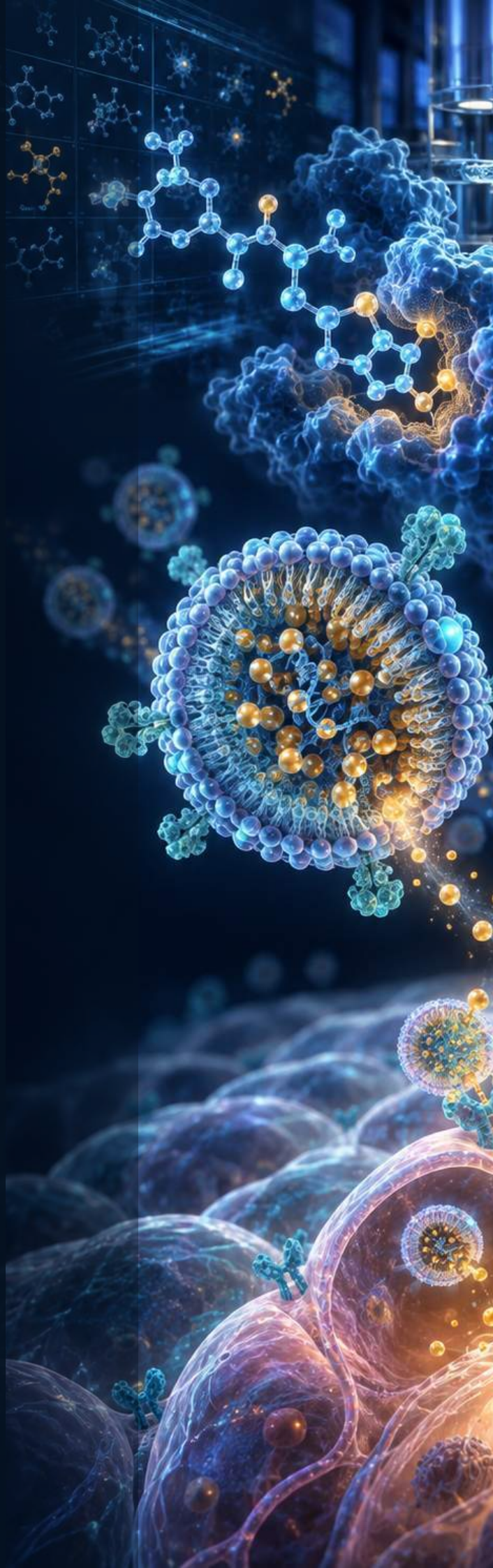
21

ANALYZED ARTICLES

10

PRIORITY THEMES

Issued 2026-10-23 | English edition | fixed approved cover artwork



Drug Discovery & DDS: the boundary moved from isolated claims to qualification evidence

21 English articles were reviewed independently from the Japanese edition. Ten themes are retained for management decisions.

SIGNAL 01 | TARGET & MOLECULE

Bepirovirsen: GSK's CHB Approval and Oligonucleotide Scale-up

The FDA has approved GSK's Hibsago (bepirovirsen) for chronic hepatitis B (CHB), demonstrating a 19% functional cure rate in pooled Phase III trials.

SIGNAL 02 | DELIVERY DESIGN

Sofusa Holdings: Lymphatic Drug Delivery Platform and 2027 FDA Timeline

Sofusa Holdings has relaunched as an independent clinical-stage company focusing on a nanotechnology platform for precision lymphatic targeting.

SIGNAL 03 | PRECLINICAL PROOF

Ultomiris: AstraZeneca's FDA accelerated approval for IgAN

AstraZeneca has received FDA accelerated approval for Ultomiris (ravulizumab) to reduce proteinuria in patients with IgA nephropathy (IgAN) at risk of progression.

SIGNAL 04 | CLINICAL DEVELOPMENT

Pembrolizumab and Enfortumab Vedotin: EC Approval for MIBC

The European Commission has approved the combination of pembrolizumab and enfortumab vedotin as perioperative treatment for adults with resectable muscle-invasive bladder cancer (MIBC).

DECISION

Focus this week's management attention on target validation, translational evidence, delivery and development economics. Move only when the linked evidence can be reproduced under your own operating conditions.

THREE MANAGEMENT MOVES

1. Buyers: separate platform promise from program-level evidence, safety and clinical differentiation.
2. Suppliers: tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.
3. Executives: track reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EVIDENCE DISCIPLINE

FACT states what the collected English source reports. BUSINESS READ and ACTION are editorial interpretations. UNKNOWN lists information that the source file does not establish. A linked article is not treated as independent confirmation of every claim.

Five numbers or evidence anchors that require conditions

19%

A01

SOURCE-BOUND CONDITION

The FDA has approved GSK's Hibsago (bepirovirsen) for chronic hepatitis B (CHB), demonstrating a 19% functional cure rate in pooled Phase III trials.

79.4%

A03

SOURCE-BOUND CONDITION

Data from the KEYNOTE-B15 trial showed a 2-year event-free survival rate of 79.4% compared to 66.2% for chemotherapy, offering a chemotherapy-free option regardless of cisplatin eligibility.

90%

A06

SOURCE-BOUND CONDITION

Researchers have developed targeted antisense oligonucleotides (ASOs) that reduce disease-causing Ataxin-3 by approximately 90% in human neurons while preserving normal protein levels.

79%

A19

SOURCE-BOUND CONDITION

PAK BioSolutions and iBET have demonstrated a continuous purification process for AAV8 that achieves 79% full-capsid enrichment over 12 hours of operation.

10%

A21

SOURCE-BOUND CONDITION

The pipeline utilizes proprietary POTENT technology to achieve oral bioavailability up to >10% and half-lives up to 8.8 days in non-human primates.

HOW TO USE THESE NUMBERS

Each value is shown with the condition stated in the collected English article. Do not compare values across different test methods, device sizes, operating temperatures or commercial stages without normalizing those conditions.

Where the value chain moved

Each stage combines one leading theme and one supporting theme. The report treats handoffs as evidence transfers, not decorative arrows.



EVIDENCE REQUIRED AT EACH HANDOFF

Target & molecule to Delivery design	Transfer test conditions, acceptance criteria, failure data, owner and decision date. Recheck reproducibility, biodistribution, toxicity, CMC, trial design and financing.
Delivery design to Preclinical proof	Transfer test conditions, acceptance criteria, failure data, owner and decision date. Recheck reproducibility, biodistribution, toxicity, CMC, trial design and financing.
Preclinical proof to Clinical development	Transfer test conditions, acceptance criteria, failure data, owner and decision date. Recheck reproducibility, biodistribution, toxicity, CMC, trial design and financing.
Clinical development to Access & portfolio	Transfer test conditions, acceptance criteria, failure data, owner and decision date. Recheck reproducibility, biodistribution, toxicity, CMC, trial design and financing.

COMMON CONTROL POINT

No theme moves to a commercial commitment until a named owner has reproduced the relevant evidence and documented reproducibility, biodistribution, toxicity, CMC, trial design and financing.

Priority map: maturity and next decision locus



REPRODUCIBLE POSITIONING RULE

Horizontal position uses five discrete stages: Research, Prototype, Joint evaluation, Product adoption and Scale. The vertical bands classify the next decision locus: Tech / process, System / adoption, or Business / rules (including supply systems). Article-title cues take precedence; the overview is used only when the title is silent. These are categories, not impact ranks. Bubble diameter reflects the editorial score.

FACT is source-bound. BUSINESS READ, ACTION and UNKNOWN are explicit editorial layers.

P01

Bepirovirsen: GSK's CHB Approval and Oligonucleotide Scale-up

A01 | Target & molecule | Scale-up

Date not stated

FACT

The FDA has approved GSK's Hibsago (bepirovirsen) for chronic hepatitis B (CHB), demonstrating a 19% functional cure rate in pooled Phase III trials. This approval marks a shift for antisense oligonucleotides from rare diseases to chronic infections affecting millions, creating significant commercial-scale manufacturing challenges for CDMOs.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P01.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 22/25 | MATURITY 5/5 | DECISION LOCUS: SYSTEM / ADOPTION

P02

Sofusa Holdings: Lymphatic Drug Delivery Platform and 2027 FDA Timeline

A20 | Delivery design | Joint evaluation

Date not stated

FACT

Sofusa Holdings has relaunched as an independent clinical-stage company focusing on a nanotechnology platform for precision lymphatic targeting. The DoseConnect platform demonstrated efficacy in rheumatoid arthritis and cutaneous lymphoma trials, with a Class II device FDA submission planned for Q2 2027.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P02.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 21/25 | MATURITY 3/5 | DECISION LOCUS: BUSINESS / RULES

FACT is source-bound. BUSINESS READ, ACTION and UNKNOWN are explicit editorial layers.

P03

Ultomiris: AstraZeneca's FDA accelerated approval for IgAN

A18 | Preclinical proof | Scale-up

Date not stated

FACT

AstraZeneca has received FDA accelerated approval for Ultomiris (ravulizumab) to reduce proteinuria in patients with IgA nephropathy (IgAN) at risk of progression. This marks the drug's fifth disease indication and establishes it as the first complement C5 inhibitor approved in the US for this rare kidney disorder.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P03.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 21/25 | MATURITY 5/5 | DECISION LOCUS: BUSINESS / RULES

P04

Pembrolizumab and Enfortumab Vedotin: EC Approval for MIBC

A03 | Clinical development | Scale-up

Date not stated

FACT

The European Commission has approved the combination of pembrolizumab and enfortumab vedotin as perioperative treatment for adults with resectable muscle-invasive bladder cancer (MIBC). Data from the KEYNOTE-B15 trial showed a 2-year event-free survival rate of 79.4% compared to 66.2% for chemotherapy, offering a chemotherapy-free option regardless of cisplatin eligibility.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P04.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 5/5 | DECISION LOCUS: SYSTEM / ADOPTION

FACT is source-bound. BUSINESS READ, ACTION and UNKNOWN are explicit editorial layers.

P05

SCA3 Therapy: Targeted ASOs Cut Toxic Ataxin-3 by 90%

A06 | Access & portfolio | Pilot

Date not stated

FACT

Researchers have developed targeted antisense oligonucleotides (ASOs) that reduce disease-causing Ataxin-3 by approximately 90% in human neurons while preserving normal protein levels. This approach utilizes Single Nucleotide Polymorphisms (SNPs) to distinguish between mutant and healthy gene copies. The findings could lead to a therapy that slows the progression of Spinocerebellar Ataxia Type 3.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P05.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 2/5 | DECISION LOCUS: TECH / PROCESS

P06

PAK BioSolutions: Integrated Continuous AAV8 Purification Specs

A19 | Target & molecule | Product adoption

Date not stated

FACT

PAK BioSolutions and iBET have demonstrated a continuous purification process for AAV8 that achieves 79% full-capsid enrichment over 12 hours of operation. The study proves that integrated capture and polishing can match the product quality of established batch processes, offering a scalable path for high-dose gene therapy manufacturing.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P06.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 4/5 | DECISION LOCUS: SYSTEM / ADOPTION

FACT is source-bound. BUSINESS READ, ACTION and UNKNOWN are explicit editorial layers.

P07

AlphaFold 3 vs BANDOCK+: Benchmarking Drug Discovery Scores

A09 | Delivery design | Pilot

Date not stated

FACT

AlphaFold 3 (AF3) demonstrates potential for computational drug discovery, achieving slightly higher aggregate disease ranking scores than BANDOCK+ in a 1,103 protein comparison. However, BANDOCK+ provides significantly broader protein coverage and lower computational demand, utilizing a 20,158 protein reference library. This highlights a critical tradeoff between predictive performance and scalability in multiscale drug discovery.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P07.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 2/5 | DECISION LOCUS: TECH / PROCESS

P08

Cellular Nanodiscs: Size-Dependent Bioactivity and Drug Delivery

A07 | Preclinical proof | Pilot

Date not stated

FACT

Researchers from the University of California San Diego found that shrinking cellular nanodiscs significantly improves their ability to bind biological targets and neutralize bacterial toxins. By comparing particles of 71, 26, and 15 nanometers, the study demonstrates that the smallest size provides the greatest protection in living systems.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P08.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 2/5 | DECISION LOCUS: TECH / PROCESS

FACT is source-bound. BUSINESS READ, ACTION and UNKNOWN are explicit editorial layers.

P09

Ascleitis Oral Peptide Pipeline: Once-Weekly Obesity Treatment Specs

A21 | Clinical development | Joint evaluation

Date not stated

FACT

Ascleitis Pharma has reported preclinical data for a once-weekly oral peptide pipeline targeting obesity and metabolic diseases, with the lead candidate ASC36o entering Phase 1 trials in the U.S. The pipeline utilizes proprietary POTENT technology to achieve oral bioavailability up to >10% and half-lives up to 8.8 days in non-human primates.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P09.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 3/5 | DECISION LOCUS: SYSTEM / ADOPTION

P10

RPT04402 Molecular Glue: Stabilizing PP2A to Suppress Cancer

A05 | Access & portfolio | Pilot

Date not stated

FACT

University of Michigan researchers have demonstrated that the molecular glue RPT04402 stabilizes the tumor-suppressing protein PP2A to inhibit cancer growth. The treatment showed efficacy in reducing tumor size in high-grade uterine cancer and delaying resistance to KRAS-targeted therapies in non-small cell lung cancer.

WHY IT MATTERS

The decision relevance is target validation, translational evidence, delivery and development economics. The signal should be tested at the application and operating-system level, not accepted from a headline alone.

BUSINESS READ

For operating companies, compare the reported change with current qualification, sourcing and product-roadmap assumptions. For suppliers, tie formulation, carriers and analytics to exposure, manufacturability and regulatory control.

ACTION

Within 30 days, separate platform promise from program-level evidence, safety and clinical differentiation; record the evidence and owner against P10.

UNKNOWN

Still unproven or incompletely stated: reproducibility, biodistribution, toxicity, CMC, trial design and financing.

EDITORIAL SCORE 20/25 | MATURITY 2/5 | DECISION LOCUS: TECH / PROCESS

Playbook and 0-5 year roadmap

STAKEHOLDER	NOW 0-30 DAYS	NEXT 1-12 MONTHS	LATER 1-5 YEARS
Operating companies	separate platform promise from program-level evidence, safety and clinical differentiation	Run production-like qualification with explicit acceptance and stop criteria.	Build a portfolio and architecture that can absorb technology and supplier changes.
Materials, equipment and technology suppliers	tie formulation, carriers and analytics to exposure, manufacturability and regulatory control	Create shared reliability, process-window and failure-analysis data with customers.	Standardize interfaces, traceability, lifecycle support and recovery services.
Trading, investment and legal teams	Map reproducibility, biodistribution, toxicity, CMC, trial design and financing.	Contract for capacity, quality, change notice, liability, alternatives and exit.	Diversify regional, technical and customer concentration risk.

ROADMAP

NOW 0-30 DAYS Evidence ledger Owner: Strategy + quality Deliverable: claim, source, condition, owner	NOW 0-30 DAYS Risk screen Owner: Procurement + legal Deliverable: unknowns, alternatives, stop	NEXT 1-12 MONTHS Joint qualification Owner: R&D + supplier Deliverable: process window and failure data
NEXT 1-12 MONTHS Commercial gate Owner: Business + finance Deliverable: unit economics and capacity	LATER 1-5 YEARS Platform strategy Owner: Executive team Deliverable: portfolio and interface roadmap	LATER 1-5 YEARS Service layer Owner: Operations + channel Deliverable: monitoring, maintenance and recovery

GO / NO-GO GATES

GATE	OWNER	REQUIRED EVIDENCE	NO-GO CONDITION
G1 Evidence	Quality	Source, test conditions and reproducibility	No traceable evidence
G2 Integration	R&D	Interface, process window and failure analysis	Cannot meet system conditions
G3 Commercial	Business	Capacity, total cost, contract and alternatives	Economics or supply cannot be supported
G4 Lifecycle	Operations	Monitoring, maintenance, change notice and exit	No accountable operating plan

ANALYZED ARTICLES | ITEMS 01-11

Every title and URL is displayed in full. URLs wrap without shortening and remain clickable. A verified-reference label means the translated HTML did not retain its original source URL.

ID	FULL ARTICLE TITLE	FULL SOURCE / VERIFIED REFERENCE URL - CLICKABLE
A01	Bepirovirsen: GSK's CHB Approval and Oligonucleotide Scale-up	https://www.pharmtech.com/view/fda-approves-bepirovirsen-why-oligonucleotide-cdmos-should-take-note
A02	Sofetabart Mipitecan: Phase 1 Efficacy and Dose Selection for HGOC	https://www.targetedonc.com/view/sofetabart-mipitecan-responses-fr-levels-ovarian-cancer
A03	Pembrolizumab and Enfortumab Vedotin: EC Approval for MIBC	https://www.onclive.com/view/pembrolizumab-plus-enfortumab-vedotin-earns-ec-approval-in-resectable-mibc
A04	Moderna and MSD: Melanoma Vaccine INTERpath-001 Phase 3 Results	https://pharmaphorum.com/news/esmo26-moderna-msd-reveal-cancer-jab-d-ata-early-after-leak
A05	RPT04402 Molecular Glue: Stabilizing PP2A to Suppress Cancer	https://www.technologynetworks.com/drug-discovery/news/stabilizing-pp2a-with-a-molecular-glue-suppresses-cancer-growth-417662
A06	SCA3 Therapy: Targeted ASOs Cut Toxic Ataxin-3 by 90%	https://www.technologynetworks.com/drug-discovery/news/targeted-asos-cut-disease-causing-ataxin-3-by-90-in-brain-disorder-417637
A07	Cellular Nanodiscs: Size-Dependent Bioactivity and Drug Delivery	https://www.technologynetworks.com/drug-discovery/news/smaller-nanodiscs-show-greater-potential-for-drug-delivery-417594
A08	RFD4-Proteina: Nvidia and UW's Open-Source Protein Design AI	https://www.genengnews.com/topics/artificial-intelligence/nvidia-uw-institute-for-protein-design-unveil-open-source-protein-design-ai-model/
A09	AlphaFold 3 vs BANDOCK+: Benchmarking Drug Discovery Scores	https://www.biorxiv.org/content/10.64898/2026.10.19.757941v2
A10	Cereblon Allosteric Inhibition: VVD-105917 and Cys287 Targeting	https://www.biorxiv.org/content/10.64898/2026.10.10.758245v1
A11	MA2 Molecular Glue: MDA5 Agonist for Innate Immunity Stimulation	https://www.biorxiv.org/content/10.64898/2026.10.14.759171v1

ANALYZED ARTICLES | ITEMS 12-21

Every title and URL is displayed in full. URLs wrap without shortening and remain clickable. A verified-reference label means the translated HTML did not retain its original source URL.

ID	FULL ARTICLE TITLE	FULL SOURCE / VERIFIED REFERENCE URL - CLICKABLE
A12	cGAS-STING/IL-12 mRNA LNPs: Systemic Tumor Control Strategy	https://www.biorxiv.org/content/10.64898/2026.10.15.759215v1
A13	KRAS-mutant CRC therapy: LNP-mediated RNAi and 5-FU synergy	https://www.biorxiv.org/content/10.64898/2026.10.15.759489v1
A14	Avian Gene Editing: LNP-Mediated Delivery for Embryo Phenotypes	https://www.biorxiv.org/content/10.64898/2026.10.13.753869v1
A15	Arrowhead ARO-MAPT: Tau reduction data and BBB platform vs Biogen	https://www.biospace.com/drug-development/arrowheads-blood-brain-barrier-tech-is-arguably-better-than-others-analysts-say-after-data-drop
A16	IDE849 (SHR-4849): Phase 1 DLL3-ADC Data for SCLC and NEC	https://www.prnewswire.com/news-releases/ide849-shr-4849-dll3-top1-adc-updated-phase-1-results-at-esmo-2026-demonstrates-promising-anti-tumor-activity-and-preliminary-overall-survival-results-in-relapsed-small-cell-lung-cancer-and-neuroendocrine-carcinomas-302917466.html
A17	Ac-FL-020: Phase 1 safety and PSA decline data for mCRPC (2026)	https://www.prnewswire.com/news-releases/full-life-technologies-reports-encouraging-preliminary-phase-1-safety-and-psa-decline-for-fl-020-in-mcrpc-at-esmo-2026-302917477.html
A18	Ultomiris: AstraZeneca's FDA accelerated approval for IgAN	https://pharmaphorum.com/news/az-grabs-fda-nod-ultomiris-rare-kidney-disease-igan
A19	PAK BioSolutions: Integrated Continuous AAV8 Purification Specs	https://www.prnewswire.com/news-releases/pak-biosolutions-and-ibet-advance-integrated-continuous-aav8-purification-302917199.html
A20	Sofusa Holdings: Lymphatic Drug Delivery Platform and 2027 FDA Timeline	https://www.biospace.com/press-releases/sofusa-holdings-relaunches-as-independent-company-to-advance-lymphatic-drug-delivery
A21	Ascletis Oral Peptide Pipeline: Once-Weekly Obesity Treatment Specs	https://biopharmaapac.com/news/31/8582/ascletis-reports-promising-preclinical-data-for-once-weekly-oral-obesity-treatments-advances-us-phase-1-trial.html

DrugDiscovery_DDS — Selected Articles

Date: 2026-10-25

Articles: 21

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- #06 SCA3 Therapy: Targeted ASOs Cut Toxic Ataxin-3 by 90%
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- #20 Sofusa Holdings: Lymphatic Drug Delivery Platform and 2027 FDA Timeline
- #21 Ascleitis Oral Peptide Pipeline: Once-Weekly Obesity Treatment Specs

#01 Bepirovirsen: GSK's CHB Approval and Oligonucleotide Scale-up

Published October 21, 2026 PharmTech USA



OVERVIEW

The FDA has approved GSK's Hibsago (bepirovirsen) for chronic hepatitis B (CHB), demonstrating a 19% functional cure rate in pooled Phase III trials. This approval marks a shift for antisense oligonucleotides from rare diseases to chronic infections affecting millions, creating significant commercial-scale manufacturing challenges for CDMOs.

Key Findings

The FDA granted priority review and Breakthrough Therapy Designation for Hibsago (bepirovirsen), an antisense oligonucleotide developed by GSK for chronic hepatitis B (CHB). In pooled data from the B-Well 1 and B-Well 2 randomized, double-blind, placebo-controlled trials across 29 countries, 19% of patients (233 of 1220) achieved a functional cure, compared to 0% of the 614 patients in the placebo group. Functional cure is defined as undetectable viral DNA and HBsAg for at least 24 weeks after treatment cessation.

Technical Details

Bepirovirsen is indicated for adults without cirrhosis who have received nucleos(t)ide analogue therapy for at least 6 months, have suppressed viral DNA, and have HBsAg levels of 3000 IU/ml or lower. The treatment consists of a 6-month course, with the option for self-administration after the first dose. Bepirovirsen works by inhibiting viral RNA production to lower viral proteins and HBsAg in the blood.

Secondary endpoints showed a 26% functional cure rate (200 of 768) in patients with baseline HBsAg of 1000 IU/ml or lower. Exploratory analyses indicated that 49% of the overall population reached HBsAg levels of 100 IU/ml or lower by week 72. Common adverse events included local pain, injection site erythema, and temporary liver enzyme increases.

Production Hurdles and Context

Scaling this modality presents significant material burdens. A 2021 Journal of Organic Chemistry perspective noted that process mass intensities for development-stage processes averaged 4299—meaning roughly 4300 kg of raw materials are required per kg of drug substance. This is significantly higher than the 168-308 kg median for small molecules. Key bottlenecks include detritylation, which consumes nearly half of synthesis-stage materials, and lyophilization, which can take several days.

Significance and Outlook

This approval expands antisense oligonucleotides into a market affecting approximately 1.7 million people in the US and over 240 million worldwide. This shift tests commercial-scale solid-phase synthesis, purification, and analytical capacity. Furthermore, the finite 6-month course alters demand forecasting, as supply will depend on new patient starts rather than lifelong maintenance.

Source: <https://www.pharmtech.com/view/fda-approves-bepirovirsen-why-oligonucleotide-cdmos-should-take-note>

Collected: October 24, 2026 | Automated Research System (AI)

#02 Sofetabart Mipitecan: Phase 1 Efficacy and Dose Selection for HGOC

Published October 22, 2026 Targeted Oncology USA



OVERVIEW

Sofetabart mipitecan demonstrated a 50.5% objective response rate in heavily pretreated high-grade ovarian cancer patients, regardless of FR α expression levels. The study identified 3 mg/kg as the recommended phase 3 dose based on a balance of efficacy and safety. These results suggest a broader therapeutic window than existing FR α -targeted ADCs.

Key Findings

In a first-in-human phase 1 study of 105 patients with high-grade ovarian cancer (HGOc), the antibody-drug conjugate (ADC) sofetabart mipitecan achieved a confirmed objective response rate (ORR) of 50.5%, including 5 complete responses and 48 partial responses. At the selected phase 3 dose of 3 mg/kg, the ORR was 58.8%. The median progression-free survival (PFS) was 8.1 months with a median follow-up of 12.9 months. Notably, the ORR was 44.4% in patients with FR α expression below 75% and 56.5% in those with expression of 75% or higher.

Technical Details

Sofetabart mipitecan (LY4170156) consists of an Fc-silent, FR α -specific humanized IgG1 antibody linked to exatecan, a topoisomerase I inhibitor, via a cleavable hydrophilic polysarcosine linker. The drug-to-antibody ratio is 8. Data indicated high stability in circulation, with less than 3% of the payload released at peak concentration.

The study evaluated doses of 2, 3, 4, and 6 mg/kg administered intravenously every 21 days. The 3 mg/kg dose was selected for the FRAmework-01 trial because it showed similar response rates to the 4 mg/kg dose but with fewer grade 3 or higher treatment-related adverse events (35.3% vs 56.4%) and fewer dose reductions (23.5% vs 41.0%).

Background and Context

FR α is overexpressed in up to 90% of ovarian cancers. Current approved FR α -targeted ADCs, such as mirvetuximab soravtansine, are restricted to patients with high expression (at least 75% of cells at 2+ intensity), covering roughly one-third of platinum-resistant ovarian cancer (PROC) patients. In contrast, this study included patients regardless of expression levels; 51.4% of participants had tumors with FR α expression below 75%. Among 19 patients previously treated with mirvetuximab soravtansine, the ORR remained 57.9%.

Significance and Outlook

The most common treatment-emergent adverse events were nausea (64.8%), fatigue (56.2%), and anemia (47.6%). No keratopathy was reported. In January 2026, the FDA granted breakthrough therapy designation to sofetabart mipitecan for platinum-resistant epithelial ovarian cancer.

Source: <https://www.targetedonc.com/view/sofetabart-mipitecan-responses-fr-levels-ovarian-cancer>

Collected: October 24, 2026 | Automated Research System (AI)

#03 Pembrolizumab and Enfortumab Vedotin: EC Approval for MIBC

Published October 21, 2026 OncLive USA



OVERVIEW

The European Commission has approved the combination of pembrolizumab and enfortumab vedotin as perioperative treatment for adults with resectable muscle-invasive bladder cancer (MIBC). Data from the KEYNOTE-B15 trial showed a 2-year event-free survival rate of 79.4% compared to 66.2% for chemotherapy, offering a chemotherapy-free option regardless of cisplatin eligibility.

Key Findings

The European Commission (EC) approved pembrolizumab (Keytruda) plus enfortumab vedotin (Padcev) for use as neoadjuvant treatment followed by adjuvant treatment after radical cystectomy in adult patients with resectable muscle-invasive bladder cancer (MIBC). This approval applies regardless of cisplatin eligibility and includes pembrolizumab and berahyaluronidase alfa (Keytruda Qlex).

In the phase 3 KEYNOTE-B15/EV-304 trial, the combination demonstrated a 2-year event-free survival (EFS) rate of 79.4% versus 66.2% for neoadjuvant gemcitabine plus cisplatin (HR, 0.53; $P < .0001$). The estimated 2-year overall survival (OS) rate was 86.9% for the combination compared to 81.3% for chemotherapy (HR, 0.65; $P = .006$). Pathologic complete response (pCR) was achieved in 55.8% of the combination group versus 32.5% in the chemotherapy group ($P < .001$).

Technical Details

The trial enrolled 808 adults with previously untreated MIBC (clinical T2-T4aN0M0 or T1-T4aN1M0) who were candidates for cisplatin and radical cystectomy. The treatment regimen for the investigational arm consisted of:

- **Neoadjuvant:** 4 cycles of intravenous pembrolizumab (200 mg on day 1) and enfortumab vedotin (1.25 mg/kg on days 1 and 8).
- **Adjuvant:** 5 cycles of enfortumab vedotin and 13 cycles of pembrolizumab following surgery.

Grade 3 or higher adverse effects (AEs) occurred in 75.7% of the combination arm versus 67.2% in the chemotherapy arm. Common reactions for the combination included rash (63%), fatigue (48%), pruritus (46%), and peripheral neuropathy (43%).

Background and Context

Cisplatin-based chemotherapy has long been the standard for MIBC, but recurrence remains a significant challenge. The FDA previously approved this combination in July 2026 for neoadjuvant and adjuvant therapy, expanding a prior indication that was limited to cisplatin-ineligible patients.

Significance and Outlook

This approval provides a meaningful advance by extending a chemotherapy-free perioperative treatment option to a broader patient population in the European Union, regardless of their ability to tolerate cisplatin.

Source: <https://www.onclive.com/view/pembrolizumab-plus-enfortumab-vedotin-earns-ec-approval-in-resectable-mibc>

Collected: October 24, 2026 | Automated Research System (AI)

#04 Moderna and MSD: Melanoma Vaccine INTerpath-001 Phase 3 Results

Published October 23, 2026 pharmaphorum UK



OVERVIEW

Moderna and MSD reported that a personalized mRNA vaccine combined with Keytruda reduced the risk of recurrence or death by 42% in patients with resected stage IIB-IV melanoma. The combination achieved a 24-month recurrence-free survival (RFS) rate of 82.2% compared to 70.0% for the control group. These results establish a new benchmark for adjuvant melanoma treatment and may accelerate Moderna's broader mRNA cancer vaccine pipeline.

Key Findings

The combination of the personalized intismeran autogene vaccine and the immunotherapy Keytruda (pembrolizumab) demonstrated a hazard ratio of 0.58, reducing the risk of recurrence or death by 42% compared to Keytruda alone at 24 months. Recurrence-free survival (RFS) at this timepoint was 82.2% for the combination group versus 70.0% for the control group. Additionally, distant metastasis-free survival (DMFS) at two years improved by 38%, reaching 88.5% in the combination group compared to 80.2% in the Keytruda-only group.

Technical Details

The intismeran autogene vaccine is developed using a personalized approach:

- Tumor sampling is used to determine the patient's unique mutational signature.
- Up to 34 cancer neoantigens—proteins appearing on tumor cells but not healthy cells—are identified.
- These antigens are used to prime the immune system to target and attack the cancer.

Safety data from the INTerpath-001 study remained consistent with previous earlier studies, and benefits were observed consistently across different patient groups.

Background and Context

The data was released early following a leak first reported by STAT and confirmed by the ESMO secretariat, ahead of the scheduled presentation at ESMO in Madrid. Following the leak, Moderna's shares fell nearly 18% and MSD shares dipped slightly. This market reaction is attributed to RFS and DMFS results being slightly lower than those seen in mid-stage trials, as well as a correction after stock gains in August.

Significance and Outlook

MSD's head of R&D, Dean Li, stated that INTERpath-001 is the first phase 3 study to show a clinically meaningful improvement in RFS and DMFS over the standard-of-care Keytruda for resected melanoma. Moderna and MSD are preparing marketing applications, with potential approvals possible next year. Beyond melanoma, this technology may pave the way for Moderna's mRNA-based vaccine pipeline currently in trials for kidney, bladder, and lung cancers.

Source: <https://pharmaphorum.com/news/esmo26-moderna-msd-reveal-cancer-jab-data-early-after-leak>

Collected: October 24, 2026 | Automated Research System (AI)

#05 RPT04402 Molecular Glue: Stabilizing PP2A to Suppress Cancer

Published October 23, 2026 Technology Networks USA



OVERVIEW

University of Michigan researchers have demonstrated that the molecular glue RPT04402 stabilizes the tumor-suppressing protein PP2A to inhibit cancer growth. The treatment showed efficacy in reducing tumor size in high-grade uterine cancer and delaying resistance to KRAS-targeted therapies in non-small cell lung cancer.

Key Findings

The molecular glue RPT04402 restores the structural stability of Protein phosphatase 2A (PP2A), a key tumor-suppressing protein, to suppress the growth of cancer cells. In mouse models of non-small cell lung cancer (NSCLC), the combination of RPT04402 with existing therapies increased treatment effectiveness to over 150 days. Additionally, RPT04402 reduced tumor growth and size in mouse uterine cancer cells and patient-derived tumor models without causing toxicity or weight loss.

Technical Details

PP2A consists of three proteins that must bind to function properly; failure to assemble is common in liver, prostate, uterine, and lung cancers. In NSCLC cases involving KRAS mutations—which occur in 30% of cases—researchers found that the FDA-approved drugs adagrasib and trametinib actually destabilize PP2A, potentially explaining why patients develop resistance. Adding RPT04402 stabilizes the PP2A complex, triggering cancer cell death and shrinking tumors in mouse models.

Background & Context

NSCLC accounts for over 80% of lung cancers, the leading cause of cancer death in the United States. While KRAS-targeting drugs exist for lung, colon, and pancreatic cancers, their efficacy is often short-lived due to acquired resistance. Similarly, high-grade uterine cancer is the deadliest gynecological malignancy, often characterized by recurrent PP2A mutations that drive aggressive growth and resistance to surgery and immunotherapy.

Significance & Outlook

This approach represents a potential new treatment for 20-30% of all NSCLC cases. The research team plans to initiate clinical trials in collaboration with Merck and Spring Works Therapeutics. Future research will evaluate whether this combination therapy is effective for other KRAS-mutant tumors, such as those in the colon and pancreas, as well as neurodevelopmental disorders involving PP2A mutations.

Collected: October 24, 2026 | Automated Research System (AI)

#06 SCA3 Therapy: Targeted ASOs Cut Toxic Ataxin-3 by 90%

Published October 22, 2026 Technology Networks Germany



OVERVIEW

Researchers have developed targeted antisense oligonucleotides (ASOs) that reduce disease-causing Ataxin-3 by approximately 90% in human neurons while preserving normal protein levels. This approach utilizes Single Nucleotide Polymorphisms (SNPs) to distinguish between mutant and healthy gene copies. The findings could lead to a therapy that slows the progression of Spinocerebellar Ataxia Type 3.

Key Findings

A research team comprising experts from DZNE, the Hertie Institute for Clinical Brain Research (HIH) at the University of Tübingen, and partners in Bonn, London, and Portugal, has successfully tested a new ASO-based approach for treating Spinocerebellar Ataxia Type 3 (SCA3). The most effective ASOs tested reduced the amount of toxic Ataxin-3 by approximately 90% in lab-cultured human neurons. Crucially, the treatment preserved the normal form of the protein, achieving a level of specificity not found in previous ASO-based therapeutic attempts.

Technical Details

The therapy targets the production chain of proteins by binding to mRNA molecules. The ASOs are designed to trigger the degradation of mRNA specifically associated with the disease-causing gene, thereby reducing the production of the harmful Ataxin-3 protein. To achieve this precision, the researchers analyzed the genomes of 79 individuals with SCA3 to identify Single Nucleotide Polymorphisms (SNPs).

- **Mechanism:** ASOs identify subtle SNP differences between the disease-causing gene copy and the healthy counterpart.
- **Selectivity:** By targeting these SNPs, the ASOs preferentially promote the degradation of mutant mRNA while leaving the healthy mRNA intact.
- **Outcome:** This allows the cell to continue producing the normal Ataxin-3 protein, which performs essential cellular functions.

Background & Context

SCA3, also known as Machado-Joseph disease, is a severe inherited neurodegenerative disorder characterized by difficulties in speech, walking, and eye movements. The disease is triggered by a genetic mutation where a specific stretch of DNA is repeated too many times, resulting in a toxic form of the Ataxin-3 protein. While humans typically have two copies of this gene, SCA3 usually involves only one mutated copy.

Significance & Outlook

The study, published in *Science Translational Medicine*, addresses a major limitation of previous ASO therapies, which often caused collateral damage by attacking healthy proteins alongside toxic ones. The team now intends to optimize the most promising ASOs and conduct further studies on efficacy and safety. The long-term objective is to move toward human clinical trials, though researchers note this process will take time.

Source: <https://www.technologynetworks.com/drug-discovery/news/targeted-asos-cut-disease-causing-ataxin-3-by-90-in-brain-disorder-417637>

Collected: October 24, 2026 | Automated Research System (AI)

#07 Cellular Nanodiscs: Size-Dependent Bioactivity and Drug Delivery

Published October 21, 2026 Technology Networks USA



OVERVIEW

Researchers from the University of California San Diego found that shrinking cellular nanodiscs significantly improves their ability to bind biological targets and neutralize bacterial toxins. By comparing particles of 71, 26, and 15 nanometers, the study demonstrates that the smallest size provides the greatest protection in living systems.

Key Findings

The smallest cellular nanodiscs consistently outperform larger versions in therapeutic performance. Experimental results show that smaller particles attach to antibodies more efficiently, interact with biological targets more rapidly, and neutralize bacterial alpha-toxin more effectively. In vivo testing on mice exposed to toxins confirmed that the smallest nanodiscs provided the highest level of protection.

Technical Details

To isolate the impact of size on biological function, the research team engineered three versions of red blood cell-derived cellular nanodiscs with diameters of approximately 71, 26, and 15 nanometers. The particles were nearly identical in all other aspects.

To explain these results, researchers utilized high-performance computing via the San Diego Supercomputer Center (SDSC) Expanse system and National Science Foundation (NSF) ACCESS allocations. Computer simulations revealed two primary drivers for the increased performance of smaller nanodiscs:

- Faster diffusion through their environment.
- A greater number of particles present for the same amount of material.

These factors combined increase the probability that the nanodiscs will encounter and bind to their intended biological targets.

Background & Context

Cellular nanodiscs are tiny particles made from natural cell membranes designed to mimic living cell functions. While their potential for vaccines, detoxification, and drug delivery was previously known, the specific influence of particle size remained an unanswered question. This interdisciplinary study involved the Halicioğlu School of Data Science and Computing and the Aiiso Yufeng Li Family Department of Chemical and Nano Engineering at UC San Diego, led by professors Liangfang Zhang and Kesong Yang.

Significance & Outlook

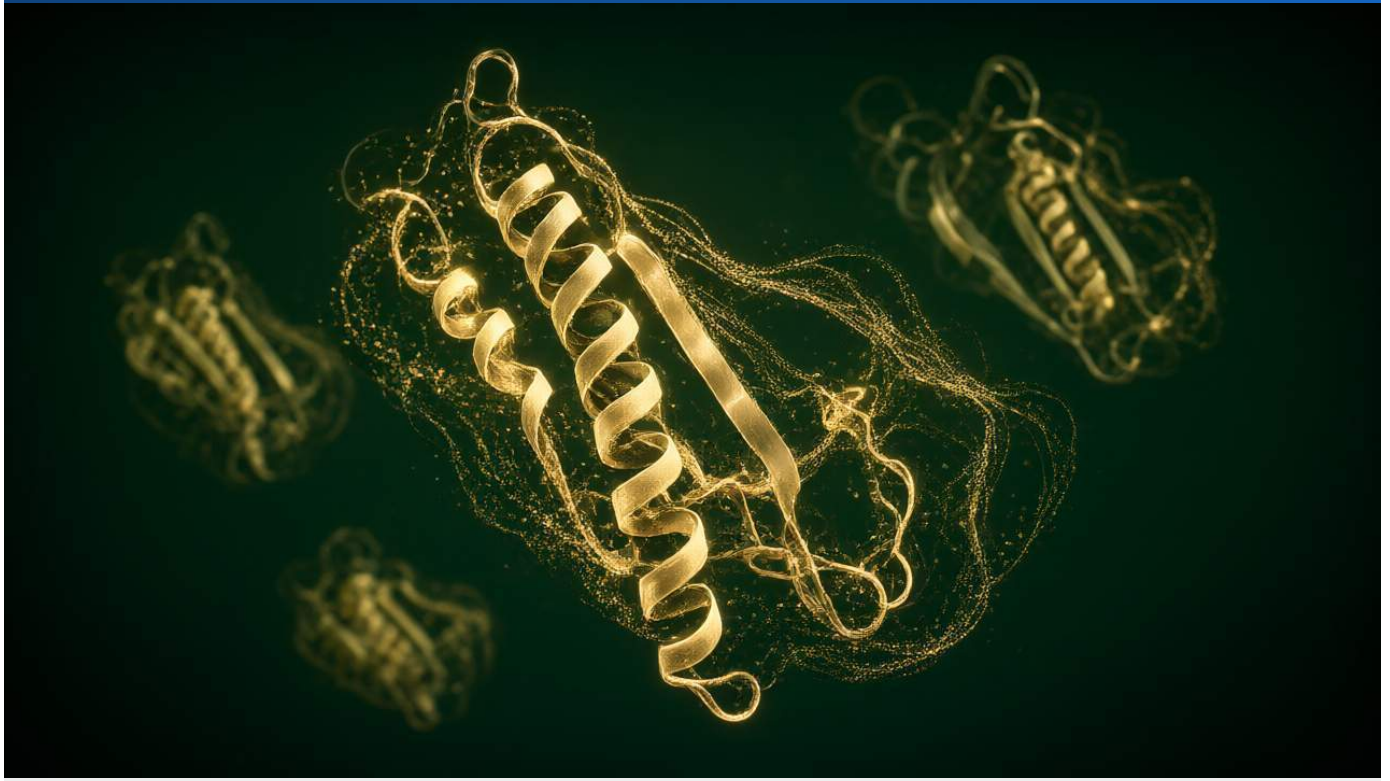
The study establishes new design principles for membrane-based therapeutics, moving away from trial-and-error experimentation toward a model that integrates simulation with laboratory validation. By identifying size as a fundamental driver of performance, this research provides a blueprint for optimizing next-generation nanomedicines for drug delivery and toxin neutralization.

Source: <https://www.technologynetworks.com/drug-discovery/news/smaller-nanodiscs-show-greater-potential-for-drug-delivery-417594>

Collected: October 24, 2026 | Automated Research System (AI)

#08 RFD4-Proteina: Nvidia and UW's Open-Source Protein Design AI

Published October 22, 2026 Genetic Engineering & Biotechnology News USA



OVERVIEW

Nvidia and the University of Washington's Institute for Protein Design (IPD) have released RFD4-Proteina, an open-source generative AI model for functional protein design. The model achieves five to 10 times higher design success rates and generation speeds compared to previous models, accelerating the development of therapeutics and sustainable materials.

Key Findings

RFD4-Proteina has demonstrated significant performance gains over previous baselines, achieving five-fold to 10-fold higher design success rates and generating protein candidates five to 10 times faster. Lab bench tests confirmed these improvements across four benchmark suites: protein binding, small-molecule binding, enzyme scaffolding, and DNA binding. Researchers reported that tasks previously taking months, such as designing a pesticide-degrading enzyme or controlling glycan attachment to proteins, were completed in under a week or a few days.

Technical Details

Built on Nvidia's NVIDIA BioNeMo™ platform, RFD4-Proteina combines programmable protein design with search capabilities. The model concurrently refines a protein's sequence and structure alongside interacting molecules, ensuring that changes in one element lead to corresponding changes in others. Its architecture derives from two primary sources: the IPD's RosettaFold Diffusion (a guided diffusion model) and Nvidia's Proteina-Complexa (a generative model for protein binder design). Proteina-Complexa utilizes a pretrained flow-based generative model built on the La-Proteina AI model for atomistic design and incorporates inference-time optimization.

Background & Context

The project was led by UW PhD students Nathaniel Corley, Maxwell Kazman, and Rafi Brent, with visiting student Kieran Didi. Funding was provided by several organizations, including the Howard Hughes Medical Institute, the Grantham Foundation, Schmidt Sciences, and the Gates Foundation, the latter of which committed \$25,748,619 via a November 2025 grant. The model is released under the Berkeley Software Distribution (BSD-3) license and is available through partners including Google Cloud, Amazon Bio Discovery, OpenAI, Anthropic's Claude Science, Hugging Face, Databricks, Benchling, Nebius, and Tamarind Bio.

Significance & Outlook

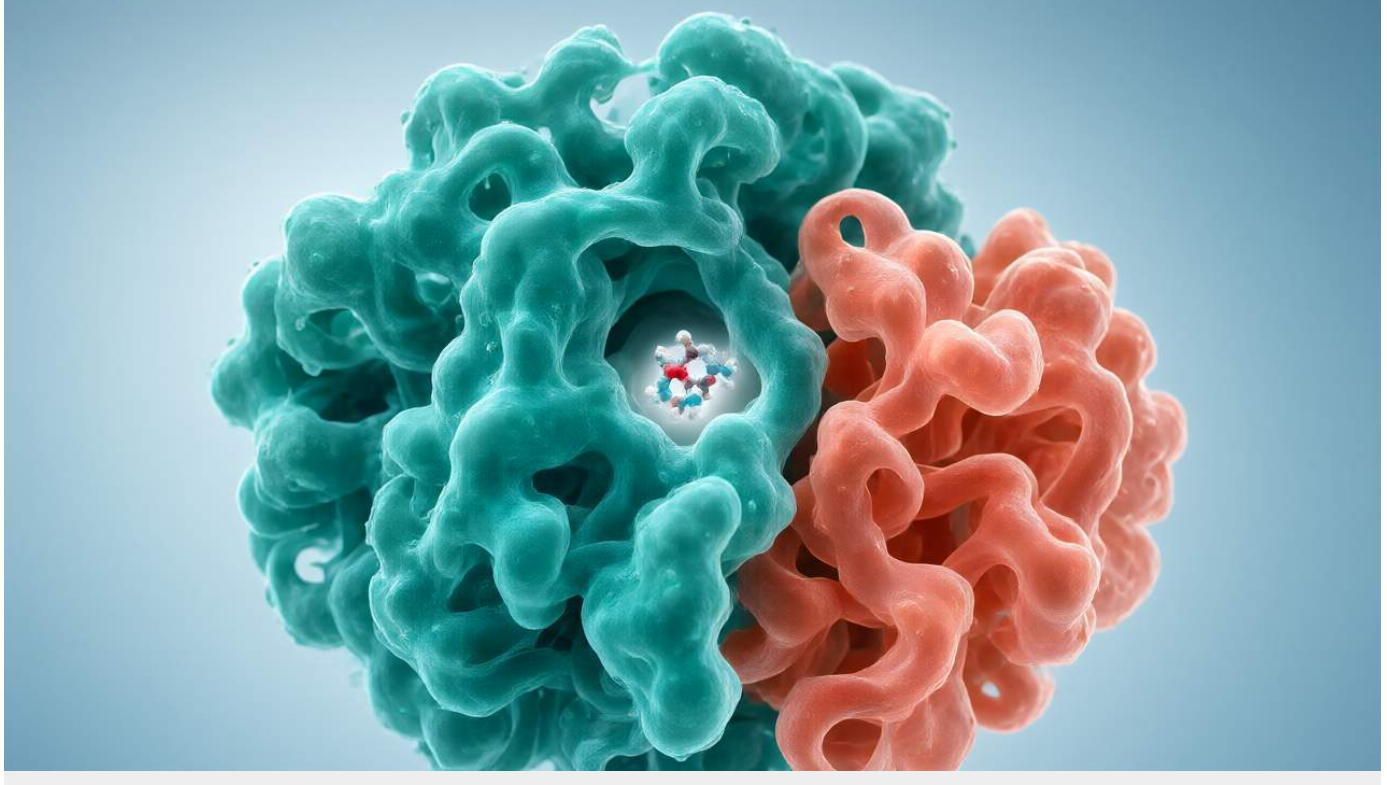
By remaining open-source, RFD4-Proteina allows researchers to prioritize candidates for lab testing more efficiently. Nobel laureate David Baker notes that the model shifts the field from discovering natural proteins to designing entirely new ones. Potential applications extend beyond medicine and drug discovery to sustainability, including the creation of bioplastics and new methods for breaking down polymers and pesticides.

Source: <https://www.genengnews.com/topics/artificial-intelligence/nvidia-uw-institute-for-protein-design-unveil-open-source-protein-design-ai-model/>

Collected: October 24, 2026 | Automated Research System (AI)

#09 AlphaFold 3 vs BANDOCK+: Benchmarking Drug Discovery Scores

Published October 22, 2026 bioRxiv



OVERVIEW

AlphaFold 3 (AF3) demonstrates potential for computational drug discovery, achieving slightly higher aggregate disease ranking scores than BANDOCK+ in a 1,103 protein comparison. However, BANDOCK+ provides significantly broader protein coverage and lower computational demand, utilizing a 20,158 protein reference library. This highlights a critical tradeoff between predictive performance and scalability in multiscale drug discovery.

Key Findings

AlphaFold 3 (AF3) confidence scores show utility in predicting protein ligand complexes, with the AF3 ipTM metric achieving slightly higher observed aggregate disease ranking scores compared to BANDOCK+ in a matched comparison of 1,103 proteins. While AF3 shows strength in predictive performance, the results vary across individual indications.

Technical Details

The study benchmarked AF3 against BANDOCK+, an experimentally informed approach, using human protein libraries and approved drugs. A primary differentiator between the two methods is scalability and computational efficiency:

- **AlphaFold 3:** Demonstrated higher ranking scores in the 1,103 protein set but requires more computational resources.
- **BANDOCK+:** Enabled substantially broader protein coverage, utilizing a reference library of 20,158 proteins while remaining computationally less demanding.

Background & Context

While AF3 is capable of predicting protein ligand complexes, the specific utility of its confidence scores for practical drug discovery applications had remained unclear. This benchmarking effort sought to clarify the performance of AF3 relative to existing experimentally informed methods like BANDOCK+ to determine where each tool fits within a drug discovery pipeline.

Significance & Outlook

The findings establish a clear tradeoff between the high-precision predictive capabilities of AF3 and the scalability of BANDOCK+. For researchers and engineers, this suggests that while AF3 confidence scores are valuable for targeted predictions, BANDOCK+ remains more viable for large-scale protein coverage due to its efficiency. The results provide a framework for choosing between predictive performance and computational scalability depending on the scope of the drug discovery project.

Source: <https://www.biorxiv.org/content/10.64898/2026.10.19.757941v2>

Collected: October 24, 2026 | Automated Research System (AI)

#10 Cereblon Allosteric Inhibition: VVD-105917 and Cys287 Targeting

Published October 15, 2026 bioRxiv USA



OVERVIEW

Researchers have identified a cryptic allosteric pocket at Cys287 of cereblon (CRBN) that can be targeted by covalent ligands to inhibit protein degradation. The lead compound, VVD-105917, traps CRBN in an inactive open conformation, providing a mechanism to override IMiD/CELMoD-driven neosubstrate degradation.

Key Findings

The study identifies a cryptic allosteric pocket distal to the orthosteric site of cereblon (CRBN) that can be engaged via covalent ligands. The lead compound, VVD-105917, acts as a pan-inhibitor of neosubstrate degradation driven by IMiDs and CELMoDs. This discovery demonstrates that the Cys287 site is mechanistically sign-switchable, as a different recently reported ligand at the same pocket promotes rather than blocks the closure of the protein.

Technical Details

Using cysteine-directed chemoproteomic screening, the researchers identified ligands that engage Cys287. Cryo-EM structures reveal that covalent engagement of Cys287 traps CRBN in an open, inactive conformation. This process resolves a sensor loop and N-terminal segment that were previously unobserved. Sequential incubation experiments indicate that the conformational outcome depends on the order in which ligands are added, proving that allosteric engagement can override the closure induced by potent CELMoDs.

Background & Context

Thalidomide-derived CRBN modulators are clinically impactful targeted protein degradation therapeutics. These agents redirect the CRL4-CRBN E3 ubiquitin ligase to degrade disease-driving neosubstrates. However, all current IMiDs and CELMoDs target a single orthosteric pocket, leaving the broader conformational landscape of CRBN largely unexplored for pharmacological use.

Significance & Outlook

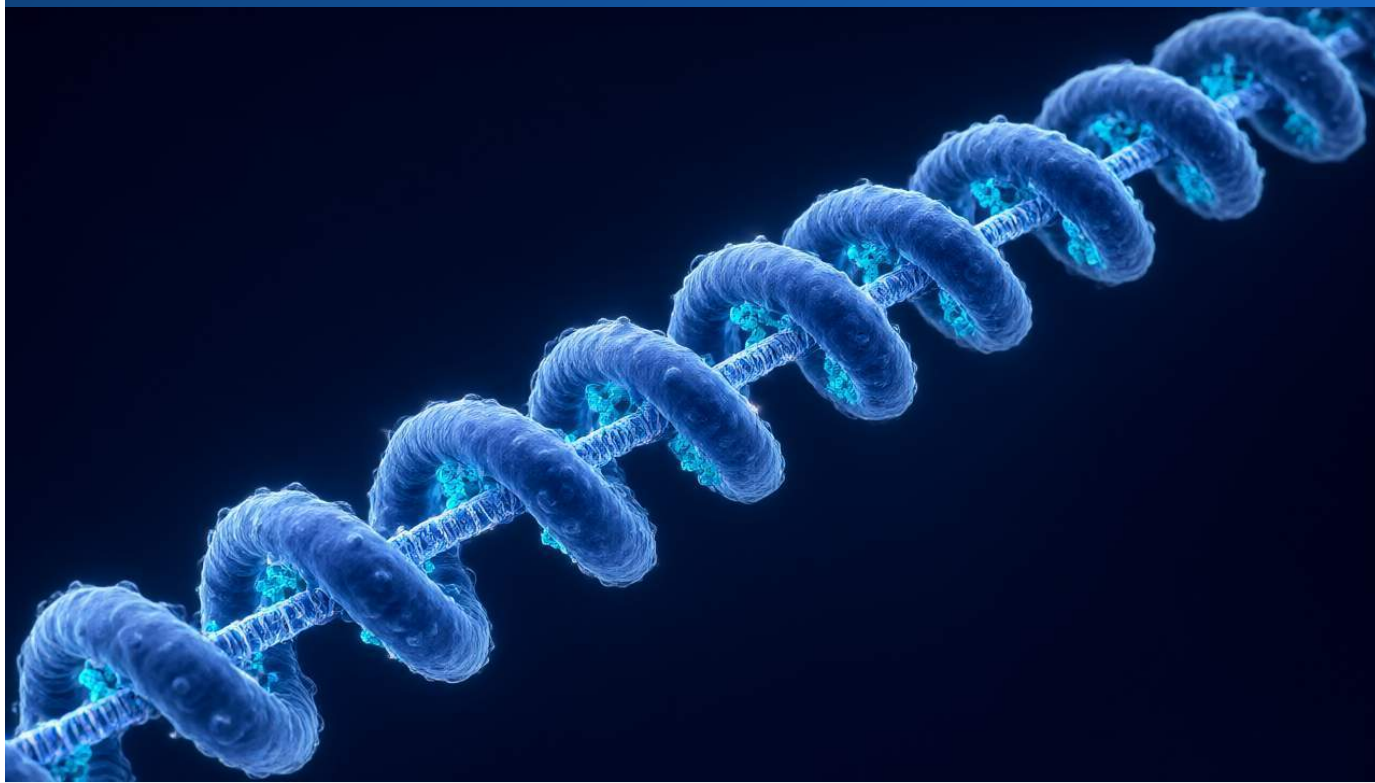
These findings establish that covalent chemoproteomics is a viable strategy for discovering and controlling conformational switches in E3 ligases. By targeting the allosteric Cys287 pocket, it is possible to modulate the activity of CRBN independently of the orthosteric site, offering a new method for controlling the degradation of neosubstrates.

Source: <https://www.biorxiv.org/content/10.64898/2026.10.10.758245v1>

Collected: October 24, 2026 | Automated Research System (AI)

#11 MA2 Molecular Glue: MDA5 Agonist for Innate Immunity Stimulation

Published October 20, 2026 bioRxiv USA



OVERVIEW

Researchers have identified MA2, a first-in-class selective MDA5 agonist that functions as a dynamic molecular glue to enhance innate immune signaling. By targeting a plastic interface within MDA5 filaments, MA2 potentiates antiviral activity and synergizes with chemotherapy and natural killer cells to improve tumor cell killing.

Key Findings

MA2 is a first-in-class selective MDA5 agonist that acts as a molecular glue to stimulate innate immunity. Unlike traditional modulators, MA2 does not induce the assembly of new filaments; instead, it potentiates pre-existing MDA5 filaments. This mechanism allows for context-dependent activation specifically in cells enriched with dsRNA. In practical applications, MA2 enhances antiviral activity and works synergistically with natural killer cells and chemotherapeutic agents to promote the killing of tumor cells.

Technical Details

The molecule targets a cryptic inter-protomer pocket within MDA5 filaments. This interface is characterized by conformational remodeling associated with ATPase activity. MA2 operates as a dynamic glue, meaning it remains bound to the interface while accommodating and reshaping structural transitions rather than locking the interface rigidly. This binding results in several biochemical effects:

- Strengthening of inter-protomer interactions.
- Strengthening of MDA5–dsRNA interactions.
- Attenuation of ATP hydrolysis.

Background & Context

MDA5 is a cytosolic dsRNA sensor responsible for activating type I interferon signaling. This signaling pathway is described as a double-edged sword: while uncontrolled activation can lead to autoinflammatory diseases, controlled activation is essential for enhancing antitumor and antiviral immunity. Despite its importance, small-molecule modulators for MDA5 have previously remained elusive due to the nature of its interfaces.

Significance & Outlook

The discovery of MA2 demonstrates that dynamic molecular glues can be used to target conformationally plastic interfaces that were previously considered undruggable. By modulating the MDA5 filament interface to enhance protective immunity, this approach provides a potential strategy for developing new therapeutic interventions in oncology and virology.

Source: <https://www.biorxiv.org/content/10.64898/2026.10.14.759171v1>

Collected: October 24, 2026 | Automated Research System (AI)

#12 cGAS-STING/IL-12 mRNA LNPs: Systemic Tumor Control Strategy

Published October 16, 2026 bioRxiv USA



OVERVIEW

Researchers have developed an mRNA lipid nanoparticle (LNP) platform that co-delivers an autoactivated cGAS mutant (R241E) and membrane-tethered IL-12 (IL-12TM) to induce systemic antitumor immunity. The combination restores effector function in tumor-infiltrating T cells and suppresses distal tumors across multiple mouse models. This approach integrates innate DNA sensing with cytokine-driven T cell programming to overcome the limitations of local tumor therapies.

Key Findings

The co-delivery of cGAS R241E and IL-12TM via mRNA LNPs promotes systemic tumor control and suppresses distal tumors in multiple mouse models. This therapeutic effect is dependent on CD8⁺ T cells and IFN- γ signaling within the host. Additionally, the combination has been shown to enhance the responsiveness of tumors to PD-L1 blockade.

Technical Details

The platform utilizes mRNA lipid nanoparticles to coordinate innate immune sensing and T cell activation in situ. The two primary components function as follows:

- **cGAS R241E:** An autoactivated mutant of cyclic GMP-AMP synthase that autonomously generates cyclic GMP-AMP in vivo, thereby activating host STING signaling and initiating antitumor responses.
- **IL-12TM:** A membrane-tethered version of interleukin-12 that promotes localized cytokine production.

Together, these components reduce the presence of regulatory T cells and restore the effector function of T cells infiltrating the tumor.

Background & Context

Local tumor therapies frequently fail to induce the systemic immunity necessary to control metastatic disease. To address this, the researchers engineered a system that couples innate DNA sensing with IL-12-mediated T cell functional reinforcement, aiming to create a more robust and widespread immune response than traditional localized treatments.

Significance & Outlook

These findings establish a clinically translatable strategy for integrating cGAS-STING activation with cytokine-driven T cell programming. By coordinating the innate and adaptive immune systems, the platform provides a mechanism to drive systemic tumor control and improve the efficacy of existing immunotherapies, such as PD-L1 blockade.

Source: <https://www.biorxiv.org/content/10.64898/2026.10.15.759215v1>

Collected: October 24, 2026 | Automated Research System (AI)

#13 KRAS-mutant CRC therapy: LNP-mediated RNAi and 5-FU synergy

Published October 16, 2026 bioRxiv



OVERVIEW

Researchers developed a lipid nanoparticle (LNP)-based RNA interference strategy using a single siRNA sequence to target KRAS G12D, G12V, and G13D mutations in colorectal cancer (CRC). The approach suppresses cellular proliferation and enhances the efficacy of 5-fluorouracil (5-FU) chemotherapy. This combination demonstrates synergistic apoptosis in both monolayer cultures and 3D spheroids.

Key Findings

The study demonstrates that a single siRNA sequence delivered via lipid nanoparticles (siRNA-LNPs) can effectively target three prevalent KRAS mutants—G12D, G12V, and G13D—to sensitize colorectal cancer (CRC) cells to chemotherapy. The combination of siRNA silencing and the fluoropyrimidine agent 5-fluorouracil (5-FU) produced synergistic effects across all three mutant models, increasing apoptosis in both monolayer cultures and 3D spheroids.

Technical Details

The siRNA-LNPs were tested across multiple cell lines to verify specificity and efficacy:

- **Targeted cells:** HCT116 (G13D), SW620 (G12V), and LS180 (G12D), where the treatment reduced KRAS mRNA and protein expression.
- **Control cells:** HT29 (KRAS wild-type), which showed no reduction in expression.

The treatment suppressed cellular proliferation, migration, and clonogenic survival. Transcriptomic profiling indicated that the siRNA-LNPs suppressed DNA repair programs and cell-cycle signaling, which provided the mechanistic rationale for the synergistic combination with 5-FU.

Background & Context

KRAS mutations, specifically G12D, G12V, and G13D, are major oncogenic drivers in CRC and are closely linked to therapeutic resistance. While KRAS inhibitors have been approved for the G12C subtype, these other prevalent variants have lacked approved targeted therapies, creating a significant gap in clinical treatment options for CRC patients.

Significance & Outlook

By utilizing a single siRNA sequence to address multiple mutation subtypes, this LNP-mediated RNAi strategy offers a versatile approach to overcoming resistance in KRAS-mutant CRC. The proof of concept established through the synergy with 5-FU supports further investigation into this combination as a potential therapeutic approach for patients with these specific oncogenic drivers.

Source: <https://www.biorxiv.org/content/10.64898/2026.10.15.759489v1>

Collected: October 24, 2026 | Automated Research System (AI)

#14 Avian Gene Editing: LNP-Mediated Delivery for Embryo Phenotypes

Published October 19, 2026 bioRxiv USA



OVERVIEW

Researchers have established a lipid nanoparticle (LNP) delivery platform for high-efficiency gene editing and phenotype generation in avian embryos. By optimizing LNP formulations, the team achieved somatic genome editing of *RUNX2* in chicken embryos, resulting in severe craniofacial ossification loss. This method provides a reproducible alternative to electroporation and viral transduction across multiple avian species.

Key Findings

The study demonstrates that lipid nanoparticle (LNP)-mediated delivery enables high-efficiency gene editing and phenotype generation in avian embryos with high viability. A primary result of this approach is the successful somatic genome editing of Runt-related transcription factor 2 (RUNX2) in chicken (*Gallus gallus*) embryos. This edit caused a severe loss and disruption of craniofacial ossification on the targeted side of the craniofacial skeleton, proving the platform's ability to produce rapid functional in vivo gene interrogation.

Technical Details

The researchers developed a robust pipeline by optimizing LNP formulation, injection timing, and frequency. The platform supports the delivery of both plasmid DNA and RNA cargos. Specifically, the system can support the piggyBac transposon system, which allows for long-term labeling of cranial neural crest cells (NCCs) and persistent reporter expression. To achieve genome editing, the team utilized RNA-based CRISPR/Cas9 components targeting migrating cranial NCCs, which are critical contributors to the craniofacial skeleton.

Background and Context

Avian embryos are valuable models for developmental biology due to the ease of observing and manipulating fertilized eggs prior to hatching. However, traditional methods such as in ovo electroporation and viral transduction are limited by variable efficiency, high embryo mortality, and procedure-induced defects. These traditional vectors have often proven ineffective for the delivery of gene editing reagents like CRISPR/Cas9.

Significance and Outlook

Beyond the chicken embryo, the study confirms that LNPs can mediate transfection in domestic pigeon (*Columba livia*) and Pekin duck (*Anas platyrhynchos*) embryos. This versatility indicates that the LNP platform can be deployed across various avian species. The ability to achieve high-viability, reproducible gene manipulation positions this technology as a viable vector delivery platform for the study of avian development, disease, and evolution.

Source: <https://www.biorxiv.org/content/10.64898/2026.10.13.753869v1>

Collected: October 24, 2026 | Automated Research System (AI)

#15 Arrowhead ARO-MAPT: Tau reduction data and BBB platform vs Biogen

Published October 15, 2026 BioSpace USA



OVERVIEW

Arrowhead Pharmaceuticals' siRNA candidate ARO-MAPT achieved up to 85% reduction in CSF tau levels in healthy volunteers, according to Phase 1/2a data. Analysts suggest the platform's ability to bypass the blood-brain barrier via subcutaneous injection may outperform competing technologies. This positions the company to compete with Biogen in the development of tau-targeting therapies.

Key Findings

Arrowhead Pharmaceuticals has released early Phase 1/2a data for ARO-MAPT, an investigational gene silencer designed to lower tau protein levels. The study in healthy volunteers demonstrated significant reductions in cerebrospinal fluid (CSF) tau, providing clinical validation for Arrowhead's platform for targeting the central nervous system through subcutaneous administration.

Technical Details

The magnitude of tau reduction varied by dose and schedule at day 105:

- **Low dose (2.1-mg/kg):** Administered on days 1, 8, and 15, resulting in an average CSF tau reduction of 40%.
- **Medium dose (6.4-mg/kg):** Administered on days 1, 8, and 15, resulting in an average reduction of 69%.
- **High dose (12.8-mg/kg):** Administered on days 1 and 15, resulting in a mean reduction of 73%, with a maximum reduction of 85% in this cohort.

Regarding safety, the treatment was generally well tolerated. Adverse events were largely mild, with no deaths, serious side effects, or dropouts due to toxicities.

Background & Context

Stifel analysts noted that these results appear more compelling than other blood-brain barrier (BBB) platforms, specifically comparing ARO-MAPT to Biogen's BII080 (diranersen). While BII080 requires direct injection into the spine, ARO-MAPT is delivered subcutaneously. Biogen's Phase 1b data for diranersen showed average CSF tau declines of 30% to 49% at eight weeks post-final dose, reaching up to 56% at 24 weeks. However, Jefferies cautioned that direct comparisons are limited due to differences in dose strengths and study populations.

Significance & Outlook

The Phase 1/2a trial is currently enrolling up to 112 participants, including healthy volunteers and patients with early Alzheimer's disease. While Biogen's Phase 2 CELIA study failed to meet its primary goal regarding cognitive and functional outcomes, Biogen intends to move diranersen into registrational development. Arrowhead expects further data on Alzheimer's disease and healthy volunteers next year and is discussing studies for progressive supranuclear palsy and MAPT-associated frontotemporal dementia with regulators.

Source: <https://www.biospace.com/drug-development/arrowheads-blood-brain-barrier-tech-is-arguably-better-than-others-analysts-say-after-data-drop>

Collected: October 24, 2026 | Automated Research System (AI)

#16 IDE849 (SHR-4849): Phase 1 DLL3-ADC Data for SCLC and NEC

Published October 23, 2026 PR Newswire (IDEAYA Biosciences) USA



OVERVIEW

IDEAYA Biosciences reported updated Phase 1 data for IDE849, a DLL3-directed ADC, showing a median overall survival (OS) of 17.4 months in second-line small cell lung cancer (SCLC). The results demonstrate significant anti-tumor activity across relapsed SCLC and neuroendocrine carcinomas (NECs), supporting the initiation of Phase 3 registrational trials.

Key Findings

IDE849 demonstrated a median OS of 17.4 months in second-line (2L) SCLC (n=51) and 14.7 months in a combined cohort of 2L and ≥ 3 L SCLC (n=101). In the 2L SCLC group, the overall response rate (ORR) was 72.5% (37/51) and the confirmed ORR (cORR) was 60.8% (31/51), with a median progression-free survival (PFS) of 6.9 months. For the combined 2L + ≥ 3 L SCLC cohort (n=101), the ORR was 68.3% (69/101) and cORR was 54.5% (55/101), with a median PFS of 6.8 months.

Technical Details

IDE849 is an antibody-drug conjugate (ADC) targeting delta-like ligand 3 (DLL3) with a topoisomerase I (TOP1) inhibitor payload. In a subgroup of SCLC patients with brain metastases, the cORR was 65.4% (17/26), and disease control was observed in all 26 patients. For other NECs (n=19), the ORR was 52.6% (10/19), cORR was 36.8% (7/19), and median PFS was 7.0 months, with a nine-month OS rate of 82.4%.

Safety data indicated a Grade ≥ 3 treatment-related adverse event (TRAE) rate of 33.3% at the 2.4 mg/kg expansion dose. Across the total study population (n=122), the treatment-related discontinuation rate was 2.5% and the Grade ≥ 3 interstitial lung disease (ILD) rate was 0.8%.

Background and Context

The data, presented at the ESMO 2026 Congress by partner Jiangsu Hengrui Pharmaceuticals, expands on 2025 WCLC findings with longer follow-up (median 12.1 months) and a larger patient population. The study included 103 SCLC patients and 19 NEC patients receiving doses ≥ 1.8 mg/kg IV every 3 weeks. Notably, 78.6% of SCLC patients had received prior immunotherapy.

Significance and Outlook

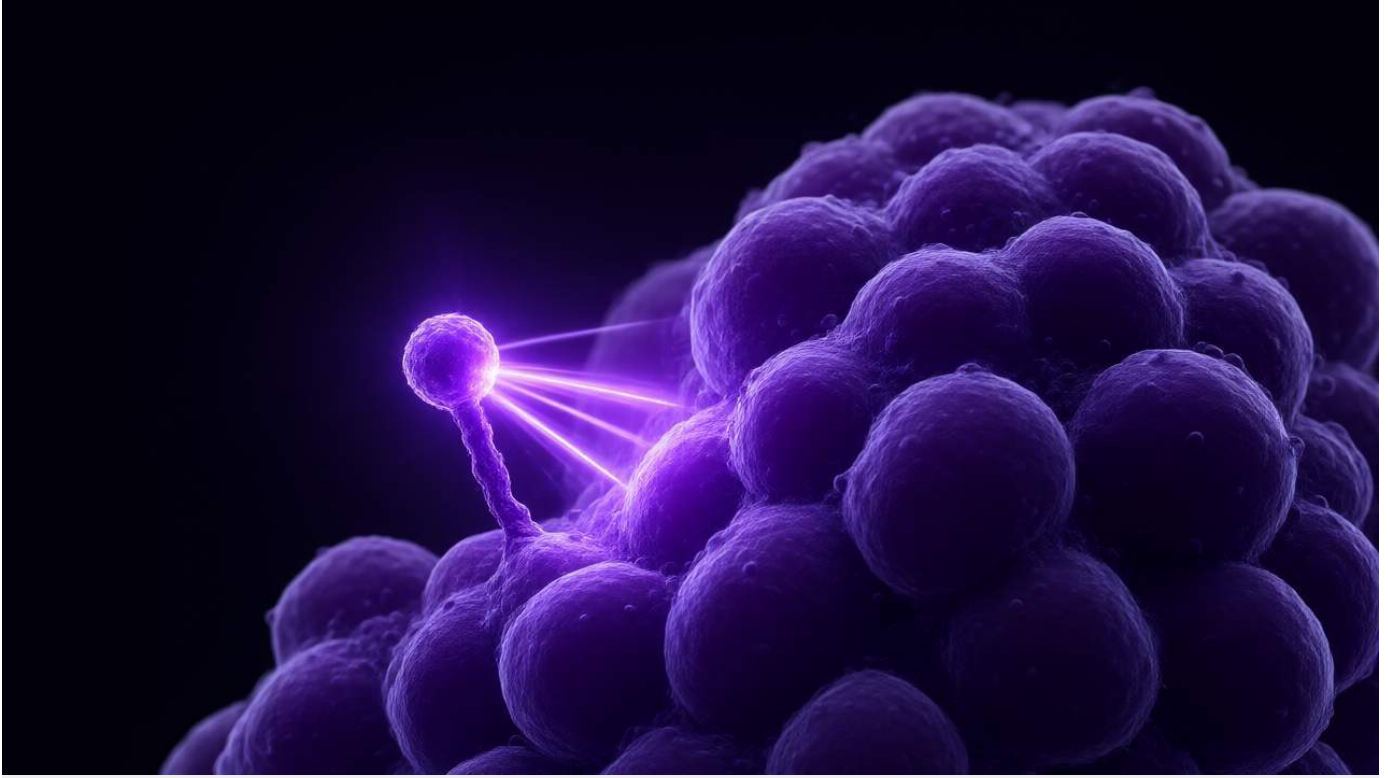
Following Type C meetings with the U.S. FDA, IDEAYA is targeting the initiation of two Phase 3 registrational trials for IDE849 in extensive-stage SCLC (ES-SCLC) and NEC. The company is also evaluating a potential Phase 3 study design for first-line ES-SCLC. IDE849 targets high unmet needs in DLL3-expressing tumors, including gastroenteropancreatic (GEP-NEC) and large cell neuroendocrine carcinomas (LC-NEC).

Source: <https://www.prnewswire.com/news-releases/ide849-shr-4849-dll3-top1-adc-updated-phase-1-results-at-esmo-2026-demonstrates-promising-anti-tumor-activity-and-preliminary-overall-survival-results-in-relapsed-small-cell-lung-cancer-and-neuroendocrine-carcinomas-302917466.html>

Collected: October 24, 2026 | Automated Research System (AI)

#17 Ac-FL-020: Phase 1 safety and PSA decline data for mCRPC (2026)

Published October 23, 2026 PR Newswire (Full-Life Technologies) USA



OVERVIEW

Full-Life Technologies reported preliminary Phase 1 data for [^{225}Ac]Ac-FL-020, showing 100% PSA50 in lutetium-177-naïve mCRPC patients at dose levels 6 to 8 MBq. The study demonstrated a promising therapeutic index with no dose-limiting toxicities, suggesting efficacy even in patients who progressed on prior lutetium-177 therapy.

Key Findings

Preliminary data from the Phase 1 dose-escalation study of [225 Ac]Ac-FL-020 indicate significant prostate-specific antigen (PSA) decline in patients with metastatic castration-resistant prostate cancer (mCRPC). In lutetium-177-naïve patients at dose levels 6 to 8 MBq, 100% achieved PSA50, 88.9% achieved PSA80, and 66.7% achieved PSA90. For lutetium-177-exposed patients at the same dose levels, PSA50 was achieved by 75%, PSA80 by 62.5%, and PSA90 by 25%.

Technical Details

The study evaluated 18 patients receiving doses of 6, 7, and 8 MBq, with 17 evaluable for PSA response. Safety data from a population of 39 patients showed no dose-limiting toxicities or deaths related to the study drug. Reported treatment-related serious adverse events included anemia, nausea, and thrombocytopenia, while no serious renal or hepatobiliary adverse events occurred. Xerostomia was predominantly Grade 1, with no Grade 3 cases. Notably, one patient who previously showed progressive disease on lutetium-177 therapy achieved a complete response via PSMA-PET imaging after two cycles of [225 Ac]Ac-FL-020 at 7 MBq.

Background & Context

[225 Ac]Ac-FL-020 is a PSMA-targeted alpha radiopharmaceutical developed using the proprietary UniRDC™ platform. It consists of a PSMA-targeting peptide labeled with actinium-225, designed for high tumor uptake and rapid clearance from normal tissue. The U.S. FDA has granted the compound Fast Track Designation for the treatment of mCRPC.

Significance & Outlook

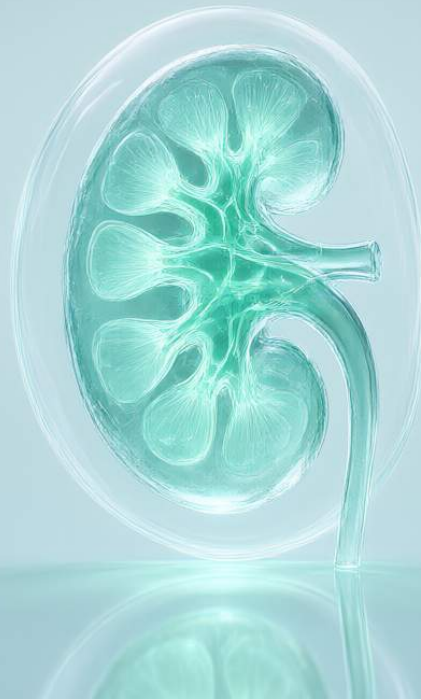
The current safety profile has supported dose escalation through 10 MBq. Full-Life Technologies plans to initiate a Phase 2 dose optimization study, randomizing patients to two dosing regimens in accordance with recent FDA draft guidance on radiopharmaceutical dose optimization. The company aims to define the optimal dose and schedule while assessing the durability of response for both lutetium-177-naive and exposed patient populations.

Source: <https://www.prnewswire.com/news-releases/full-life-technologies-reports-encouraging-preliminary-phase-1-safety-and-psa-decline-for-fl-020-in-mcrpc-at-esmo-2026-302917477.html>

Collected: October 24, 2026 | Automated Research System (AI)

#18 Ultomiris: AstraZeneca's FDA accelerated approval for IgAN

Published October 22, 2026 pharmaphorum UK



OVERVIEW

AstraZeneca has received FDA accelerated approval for Ultomiris (ravulizumab) to reduce proteinuria in patients with IgA nephropathy (IgAN) at risk of progression. This marks the drug's fifth disease indication and establishes it as the first complement C5 inhibitor approved in the US for this rare kidney disorder.

Key Findings

AstraZeneca has secured FDA accelerated approval for Ultomiris in the treatment of IgA nephropathy (IgAN). The drug is indicated to reduce proteinuria, which serves as a marker for kidney function and a surrogate marker for disease activity in patients at risk of progression. This approval follows the results of the phase 3 I CAN trial.

Technical Details

Ultomiris is a complement C5 inhibitor. In the I CAN trial, patients received a loading dose followed by infusions every eight weeks. At 34 weeks, this regimen resulted in a 43.4% reduction in proteinuria compared to the placebo group. Because the approval is accelerated, AstraZeneca must provide additional data from the I CAN trial to demonstrate that the reduction in proteinuria correlates with a slowdown in the decline of kidney function. The study is currently tracking the estimated glomerular filtration rate (eGFR) over a period of 106 weeks to support full FDA approval.

Background & Context

IgAN is a rare disorder characterized by the accumulation of antibodies in the kidneys, leading to inflammation, scarring, and potential chronic kidney disease (CKD). It is the most common primary glomerulonephritis globally, affecting between 25 and 50 people per million annually, with an estimated 200,000 patients in the US. Ultomiris is already approved for four other conditions: paroxysmal nocturnal haemoglobinuria, atypical haemolytic uraemic syndrome (HUS), generalised myasthenia gravis (gMG), and neuromyelitis optica spectrum disorder (NMOSD). In the first six months of the year, the drug generated revenues of \$2.58 billion.

Significance & Outlook

The IgAN market is seeing a surge in activity, with six new therapies reaching the US market in the last decade. AstraZeneca is also pursuing regulatory submissions for Ultomiris in Japan and other countries based on interim I CAN results. Additionally, the company is testing the drug for haematopoietic stem cell transplant-associated thrombotic microangiopathy (HSCT-TMA), with regulatory filings currently in progress.

Source: <https://pharmaphorum.com/news/az-grabs-fda-nod-ultomiris-rare-kidney-disease-igan>

Collected: October 24, 2026 | Automated Research System (AI)

#19 PAK BioSolutions: Integrated Continuous AAV8 Purification Specs

Published October 22, 2026 PR Newswire (PAK BioSolutions) USA



OVERVIEW

PAK BioSolutions and iBET have demonstrated a continuous purification process for AAV8 that achieves 79% full-capsid enrichment over 12 hours of operation. The study proves that integrated capture and polishing can match the product quality of established batch processes, offering a scalable path for high-dose gene therapy manufacturing.

Key Findings

A peer-reviewed study published in *Separation and Purification Technology* reports that the PAK PD™ Process Development Scale Continuous Purification System can maintain reproducible AAV8 purification for 12 hours. The integrated process achieved a final full-capsid enrichment of 79%, starting from 34% after the initial affinity capture. Vector genome recovery from feed to final pool was 44%.

Technical Details

The research team, collaborating with iBET (Instituto de Biologia Experimental e Tecnológica), implemented a cyclic integrated capture–polishing chromatography workflow. The technical configuration included:

- **Capture Stage:** AAVX affinity capture using two alternating columns.
- **Polishing Stage:** Mustang® Q anion-exchange membrane polishing using two alternating columns.
- **Automation:** The PAK system coordinated column switching, inline dilution of capture eluate, and parallel transfer between stages.
- **Impurity Reduction:** dsDNA was reduced to below the assay detection limit after capture, and host cell protein was reduced to below the detection limit after polishing.

The final full-capsid content of 79% is consistent with the 68–81% range typically reported for batch anion-exchange polishing of AAV8.

Background and Context

As in vivo gene therapies move toward commercialization, higher dosing requirements necessitate increased throughput without sacrificing quality. While continuous operation has previously been limited to individual steps—typically pairing continuous capture with batch polishing—this study integrates both into a single continuous process. This builds on PAK BioSolutions' previous work with monoclonal antibodies (mAbs), including a 14-day integrated run with AstraZeneca.

Significance and Outlook

The study demonstrates that batch AAV purification workflows can be translated into an integrated continuous format through defined process adaptation, without requiring bespoke system engineering. The PAK system architecture—spanning the PAK PD™, PAK Pilot™, and PAK K-Series™—allows these processes to transition from development to commercial manufacturing on the same technology platform.

Source: <https://www.prnewswire.com/news-releases/pak-biosolutions-and-ibet-advance-integrated-continuous-aav8-purification-302917199.html>

Collected: October 24, 2026 | Automated Research System (AI)

#20 Sofusa Holdings: Lymphatic Drug Delivery Platform and 2027 FDA Timeline

Published October 23, 2026 BioSpace (Business Wire配信) USA



OVERVIEW

Sofusa Holdings has relaunched as an independent clinical-stage company focusing on a nanotechnology platform for precision lymphatic targeting. The DoseConnect platform demonstrated efficacy in rheumatoid arthritis and cutaneous lymphoma trials, with a Class II device FDA submission planned for Q2 2027.

Key Findings

Sofusa Holdings is advancing the DoseConnect platform, which utilizes nanotopography-draped microneedles to deliver biologic therapies directly into the lymphatic system. In a Phase 1b study of 10 patients with moderate-to-severe rheumatoid arthritis who failed to improve on 50 mg of subcutaneous etanercept, switching to lymphatic delivery at a reduced dose of 25 mg resulted in a 70% reduction in tender joints, a 62% reduction in pain, and a 34% improvement in DAS28-ESR. Additionally, in a Phase 1b study at City of Hope for cutaneous T-cell lymphoma (CTCL), two of three patients with advanced disease responded to lymphatic delivery of pembrolizumab after failing prior treatments.

Technical Details

The platform targets the lymphatic vessels and lymph nodes where key immune targets reside. Preclinical biodistribution studies indicate that this method achieves up to 80-fold higher drug concentrations in lymph nodes compared to conventional subcutaneous administration, while maintaining lower concentrations in off-target organs. Because the system is compatible with already-approved biologic medicines, the company expects a more efficient development pathway with reduced costs and timelines. Potential applications include bispecific antibodies and oncolytic virus therapies to reduce systemic toxicity.

Background and Context

The technology was originally developed at Kimberly-Clark and further advanced through clinical trials under Sorrento Therapeutics, with cumulative investment totaling approximately \$100 million. New investors have since acquired the rights to launch Sofusa as an independent entity. The company has restarted manufacturing to develop a pipeline for autoimmune diseases, cancer, and other immune system disorders.

Significance and Outlook

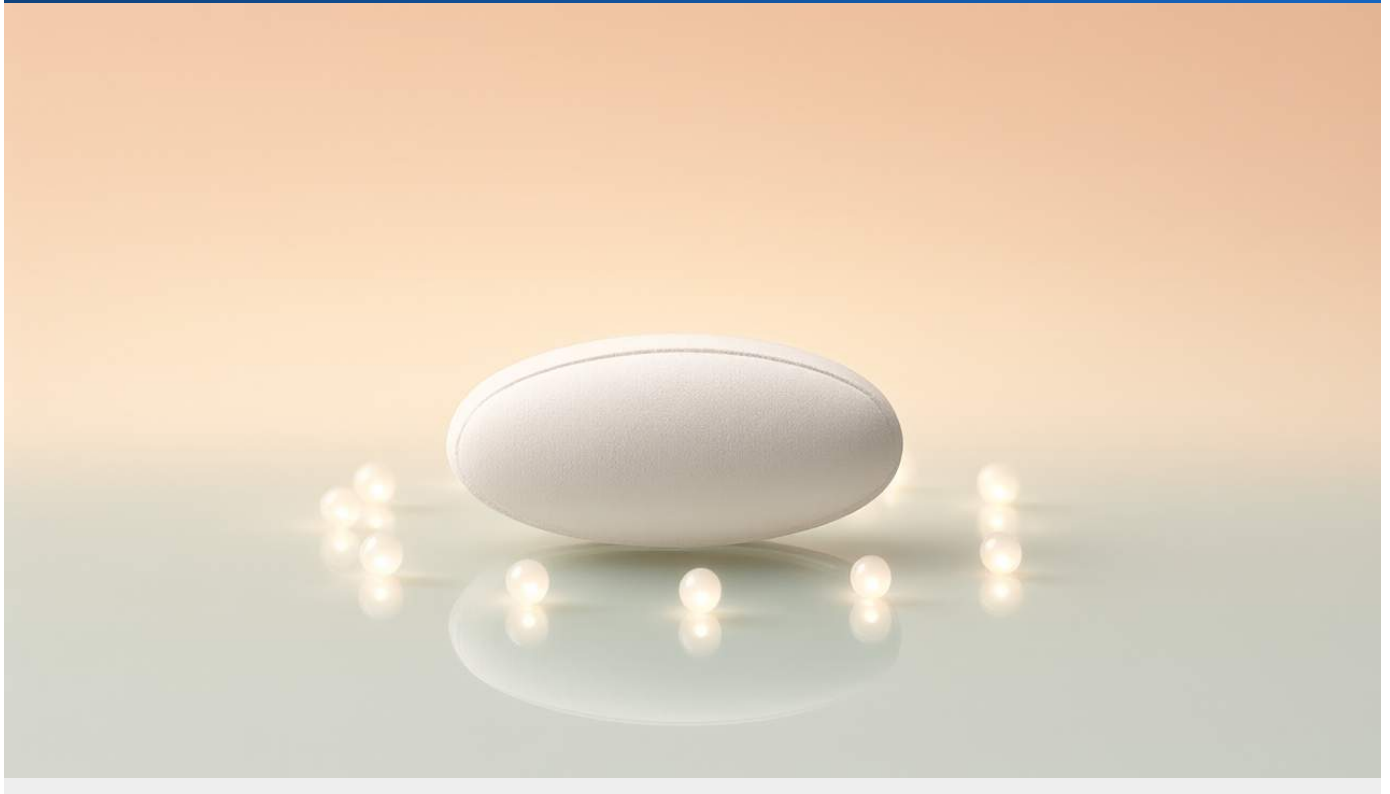
Sofusa plans to submit its first FDA application for a Class II device for intradermal delivery of biologics in Q2 2027. The company's leadership emphasizes that direct access to the lymphatic network may allow for lower drug dosages to achieve superior therapeutic outcomes. Sofusa will present further details at the MedTech Strategist Innovation Summit in San Diego on November 4, 2026.

Source: <https://www.biospace.com/press-releases/sofusa-holdings-relaunches-as-independent-company-to-advance-lymphatic-drug-delivery>

Collected: October 24, 2026 | Automated Research System (AI)

#21 Ascletis Oral Peptide Pipeline: Once-Weekly Obesity Treatment Specs

Published October 21, 2026 BioPharma APAC China



OVERVIEW

Ascletis Pharma has reported preclinical data for a once-weekly oral peptide pipeline targeting obesity and metabolic diseases, with the lead candidate ASC36o entering Phase 1 trials in the U.S. The pipeline utilizes proprietary POTENT technology to achieve oral bioavailability up to >10% and half-lives up to 8.8 days in non-human primates.

Key Findings

Ascletis Pharma has advanced its lead candidate, ASC36o, a once-weekly oral amylin receptor peptide agonist, into a Phase 1 study in the U.S. Preclinical data in non-human primates (NHPs) shows ASC36o has a half-life of up to 167 hours (approximately 7 days) and oral bioavailability between 6% and 8%. In diet-induced obesity (DIO) rat studies, ASC36o demonstrated body weight reduction 32% and 91% greater than eloralintide and petrelintide, respectively.

Technical Details

The company's pipeline leverages Peptide Oral Transport ENhancement Technology (POTENT), which increases oral bioavailability via both gastric and intestinal absorption while reducing within-subject and between-subject variability. This technology supports several configurations:

- **ASC36o:** Amylin receptor peptide agonist.
- **ASC36_35o FDC:** A fixed-dose combination (FDC) of amylin receptor, GLP-1R, and GIPR agonists. In NHPs, this combination increased the half-life of ASC36o to approximately 8.8 days (up to 212 hours) and bioavailability to $\geq 10\%$.
- **ASC36_37o FDC:** A quadruple peptide agonist (amylin receptor, GLP-1R, GIPR, and GCGR). In NHPs, this combination showed a half-life of approximately 8.3 days (up to 200 hours) and bioavailability of $\geq 10\%$.
- **ASC35o and ASC37o:** Once-weekly oral dual (GLP-1/GIP) and triple (GLP-1/GIP/GCG) peptide agonists, respectively.

Background and Context

The pipeline is designed to cover all four validated targets for obesity and metabolic diseases: amylin, GLP-1, GIP, and GCG receptors. By combining these targets into single-pill FDCs, Ascletis intends to expand the population treatable with oral agents compared to single-agent therapies.

Significance and Outlook

The combination of high oral bioavailability and extended half-lives is intended to make once-weekly oral dosing commercially viable. Ascletis expects to receive topline human pharmacokinetic data for ASC360 by the end of 2026. Additionally, the company expects to submit Investigational New Drug (IND) applications to the FDA for its four other once-weekly oral peptide programs in the fourth quarter of 2026.

Source: <https://biopharmaapac.com/news/31/8582/ascletis-reports-promising-preclinical-data-for-once-weekly-oral-obesity-treatments-advances-us-phase-1-trial.html>

Collected: October 24, 2026 | Automated Research System (AI)