TROY TECHNICAL

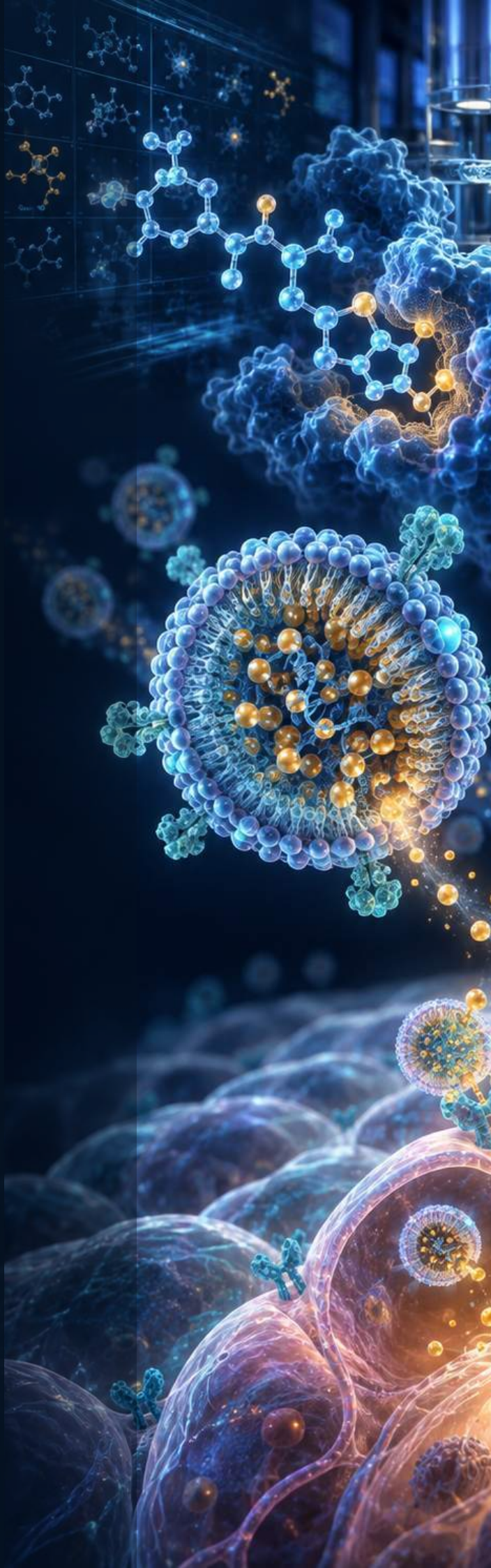
DRUG DISCOVERY & DDS
WEEKLY REPORT

October 24 - October 30, 2026 | Issue 2026-W43

Target validation, translational evidence, delivery and development economics

15	10
ANALYZED ARTICLES	PRIORITY THEMES

Issued 2026-10-30 | English edition | fixed approved cover artwork



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

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

SIGNAL 01 | TARGET & MOLECULE

pro-DALAP Platform: Yeast-Based Oral Dual GLP-1/GIP Agonist Evaluation

Researchers developed a Saccharomyces cerevisiae-based platform to deliver pro-DALAP, a dual GLP-1/GIP receptor agonist, via oral enteric-coated capsules.

SIGNAL 02 | DELIVERY DESIGN

Amgen Imdelltra: Phase 3 DeLLphi-305 results for ES-SCLC

Amgen's Imdelltra, combined with AstraZeneca's Imfinzi, reduced the risk of death by 58% compared to Imfinzi alone in first-line maintenance treatment for extensive-stage small cell lung cancer (ES-SCLC).

SIGNAL 03 | PRECLINICAL PROOF

JNJ-6143: Phase 1 results for RIPTAC in advanced prostate cancer

Johnson & Johnson reported a 75% complete or partial tumor response rate in patients with advanced prostate cancer treated with JNJ-6143. The once-daily oral molecule demonstrated significant PSA reductions in patients who had failed multiple prior therapies.

SIGNAL 04 | CLINICAL DEVELOPMENT

FDA Gene Editing Guidance: BLA Process and IFS for Rare Diseases

The FDA has issued draft guidance allowing biologics license applications (BLAs) for individualized genome editing products to add patient-specific variants without new clinical trials.

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

58%	A06	SOURCE-BOUND CONDITION Amgen's Imdelltra, combined with AstraZeneca's Imfinzi, reduced the risk of death by 58% compared to Imfinzi alone in first-line maintenance treatment for extensive-stage small cell lung cancer (ES-SCLC).
75%	A13	SOURCE-BOUND CONDITION Johnson & Johnson reported a 75% complete or partial tumor response rate in patients with advanced prostate cancer treated with JNJ-6143.
1.7%	A09	SOURCE-BOUND CONDITION Ascletis Pharma's oral small molecule GLP-1 receptor agonist, ASC30, achieved a placebo-adjusted HbA1c reduction of up to 1.7% and weight loss of up to 4.4% in a U.S.
20.5%	A07	SOURCE-BOUND CONDITION With an objective response rate of 20.5% in the efficacious exposure group, the study establishes clinical proof of concept for B7-H4 as a viable ADC target.
45.5%	A08	SOURCE-BOUND CONDITION Xencor has selected 400 mcg/kg as the proposed IV recommended Phase 3 dose (RP3D) for XmAb819, showing a 45.5% cORR and 82% 6-month PFS estimate.

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.

1

Target & molecule

P01/P06

Researchers developed a Saccharomyces cerevisiae-based platform to deliver pro-DALAP, a dual GLP-1/GIP receptor agonist, via.

2

Delivery design

P02/P07

Amgen's Imdelltra, combined with AstraZeneca's Imfinzi, reduced the risk of death by 58% compared to Imfinzi alone in.

3

Preclinical proof

P03/P08

Johnson & Johnson reported a 75% complete or partial tumor response rate in patients with advanced prostate cancer treated.

4

Clinical development

P04/P09

The FDA has issued draft guidance allowing biologics license applications (BLAs) for individualize d genome editing products.

5

Access & portfolio

P05/P10

Ascletis Pharma's oral small molecule GLP-1 receptor agonist, ASC30, achieved a placebo-adjusted HbA1c reduction of up to.

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



P01	pro-DALAP Platform: Yeast-Based Oral Dual GLP-1/GIP Agonist Evaluation System / adoption | cue: Platform
P02	Amgen Imdelltra: Phase 3 DeLLphi-305 results for ES-SCLC System / adoption | cue: Phase 3
P03	JNJ-6143: Phase 1 results for RIPTAC in advanced prostate cancer System / adoption | cue: Phase 1
P04	FDA Gene Editing Guidance: BLA Process and IFS for Rare Diseases Business / rules | cue: FDA
P05	Ascletis ASC30: Phase II Results for Oral GLP-1 in Type 2 Diabetes System / adoption | cue: trial
P06	AZD8205: B7-H4 ADC Phase 1/2a results for solid tumors System / adoption | cue: Phase 1
P07	FDA Gene Therapy Guidance: Expediting Personalized BLA Approvals Business / rules | cue: FDA
P08	XmAb819: Phase 1 Dose Selection and ccRCC Development Roadmap System / adoption | cue: Phase 1
P09	CAMOLE-1: ML-driven discovery of selective MMP12 inhibitors System / adoption | cue: platform
P10	MAGEA11-Recruiting PROTACs: Cancer-Selective BET Degradation Tech / process | cue: no system/business cue

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 pro-DALAP Platform: Yeast-Based Oral Dual GLP-1/GIP Agonist Evaluation

A03 | Target & molecule | Joint evaluation

Date not stated

FACT

Researchers developed a Saccharomyces cerevisiae-based platform to deliver pro-DALAP, a dual GLP-1/GIP receptor agonist, via oral enteric-coated capsules. While in vitro and rat toxicology studies showed functionality and safety, a 12-week clinical trial in overweight adults did not yield statistically significant differences in body weight or waist circumference compared to dietary guidance.

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

P02 Amgen Imdelltra: Phase 3 DeLLphi-305 results for ES-SCLC

A06 | Delivery design | Research

Date not stated

FACT

Amgen's Imdelltra, combined with AstraZeneca's Imfinzi, reduced the risk of death by 58% compared to Imfinzi alone in first-line maintenance treatment for extensive-stage small cell lung cancer (ES-SCLC). The combination extended median overall survival to 21.1 months, potentially expanding the drug's U.S. addressable patient population to approximately 21,600.

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 20/25 | MATURITY 1/5 | DECISION LOCUS: SYSTEM / ADOPTION

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

P03 JNJ-6143: Phase 1 results for RIPTAC in advanced prostate cancer

A13 | Preclinical proof | Joint evaluation

Date not stated

FACT

Johnson & Johnson reported a 75% complete or partial tumor response rate in patients with advanced prostate cancer treated with JNJ-6143. The once-daily oral molecule demonstrated significant PSA reductions in patients who had failed multiple prior therapies. These results support the advancement of the 50-mg dose into Phase 2 clinical trials.

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

P04 FDA Gene Editing Guidance: BLA Process and IFS for Rare Diseases

A11 | Clinical development | Product adoption

Date not stated

FACT

The FDA has issued draft guidance allowing biologics license applications (BLAs) for individualized genome editing products to add patient-specific variants without new clinical trials. By shifting the evidentiary burden to CMC assay data and the "Individualized Feature Space" (IFS), the framework accelerates access to therapies for ultrarare genetic diseases.

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 4/5 | DECISION LOCUS: BUSINESS / RULES

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

P05 Ascletis ASC30: Phase II Results for Oral GLP-1 in Type 2 Diabetes

A09 | Access & portfolio | Joint evaluation

Date not stated

FACT

Ascletis Pharma's oral small molecule GLP-1 receptor agonist, ASC30, achieved a placebo-adjusted HbA1c reduction of up to 1.7% and weight loss of up to 4.4% in a U.S. Phase II trial for type 2 diabetes. The drug demonstrated favorable gastrointestinal tolerability with zero discontinuations due to GI adverse events. These results position ASC30 as a potential once-daily oral treatment for both diabetes and obesity.

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 3/5 | DECISION LOCUS: SYSTEM / ADOPTION

P06 AZD8205: B7-H4 ADC Phase 1/2a results for solid tumors

A07 | Target & molecule | Joint evaluation

Date not stated

FACT

The first-in-human BLUESTAR trial of the B7-H4-directed antibody-drug conjugate AZD8205 (puxitatug samrotecan) demonstrated partial tumor responses in patients with advanced ovarian, endometrial, and breast cancers. With an objective response rate of 20.5% in the efficacious exposure group, the study establishes clinical proof of concept for B7-H4 as a viable ADC target.

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 3/5 | DECISION LOCUS: SYSTEM / ADOPTION

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

P07 FDA Gene Therapy Guidance: Expediting Personalized BLA Approvals

A10 | Delivery design | Research

Date not stated

FACT

The FDA and CMS have introduced a draft guidance allowing a single Biologics License Application (BLA) to cover multiple personalized gene therapy variants. This framework, combined with the expansion of the CMS Cell and Gene Therapy Access Model, aims to accelerate patient access to treatments for ultra-rare diseases.

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 1/5 | DECISION LOCUS: BUSINESS / RULES

P08 XmAb819: Phase 1 Dose Selection and ccRCC Development Roadmap

A08 | Preclinical proof | Research

Date not stated

FACT

Xencor has selected 400 mcg/kg as the proposed IV recommended Phase 3 dose (RP3D) for XmAb819, showing a 45.5% cORR and 82% 6-month PFS estimate. The company plans to discuss an accelerated FDA approval pathway in 1H2027 for specific advanced clear cell renal cell carcinoma (ccRCC) subgroups.

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 19/25 | MATURITY 1/5 | DECISION LOCUS: SYSTEM / ADOPTION

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

P09 CAMOLE-1: ML-driven discovery of selective MMP12 inhibitors

A04 | Clinical development | Pilot

Date not stated

FACT

Calico Life Sciences developed CAMOLE-1, a machine learning platform that utilizes an all-atom diffusion model to design potent and selective peptide inhibitors. The system successfully optimized an MMP12 inhibitor over approximately one year through the synthesis of 270 peptides. This approach demonstrates the ability of ML to drive peptide design from initial hit discovery to lead development with improved pharmacokinetic properties.

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 19/25 | MATURITY 2/5 | DECISION LOCUS: SYSTEM / ADOPTION

P10 MAGEA11-Recruiting PROTACs: Cancer-Selective BET Degradation

A14 | Access & portfolio | Pilot

Date not stated

FACT

Researchers have developed the first PROTAC that recruits the tissue-specific E3 ligase scaffolding protein MAGEA11 to achieve cancer-restricted protein degradation. Lead compound 105B degrades BET proteins in osteosarcoma and esophageal squamous cell carcinoma cells while showing no degradation in non-cancerous HEK293T cells. This approach provides a strategy to increase the therapeutic window by targeting E3 ligases overexpressed in specific tissues.

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 19/25 | 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 01-15

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	LNP Morphology: Impact of Shape on mRNA Transfection Performance	https://www.biorxiv.org/content/10.64898/2026.10.18.759824v1
A02	Light-Responsive LNPs: VEGFA Editing for CNV Suppression	https://www.biorxiv.org/content/10.64898/2026.10.24.761602v1
A03	pro-DALAP Platform: Yeast-Based Oral Dual GLP-1/GIP Agonist Evaluation	https://www.medrxiv.org/content/10.64898/2026.10.22.26365662v1
A04	CAMOLE-1: ML-driven discovery of selective MMP12 inhibitors	https://www.biorxiv.org/content/10.64898/2026.10.21.755545v1
A05	ZW191 Phase 1 Data: FRα-Targeting ADC Efficacy in PROC Patients	https://www.biospace.com/press-releases/zymeworks-presents-new-phase-1-data-for-folate-receptor-alpha-targeting-antibody-drug-conjugate-zw191-at-esmo-congress-2026
A06	Amgen Imdelltra: Phase 3 DeLLphi-305 results for ES-SCLC	https://www.biospace.com/drug-development/esmo-2026-amgens-imdelltra-slashes-death-risk-by-nearly-60-in-small-cell-lung-cancer
A07	AZD8205: B7-H4 ADC Phase 1/2a results for solid tumors	https://bioengineer.org/first-in-human-trial-shows-b7-h4-antibody-drug-conjugate-shrinks-ovarian-endometrial-and-breast-tumors/
A08	XmAb819: Phase 1 Dose Selection and ccRCC Development Roadmap	https://finance.yahoo.com/healthcare/articles/xencor-presents-phase-1-dose-083500804.html
A09	Ascletis ASC30: Phase II Results for Oral GLP-1 in Type 2 Diabetes	https://biopharmaapac.com/news/31/8617/ascletis-oral-glp-1-asc30-delivers-up-to-1-7-hba1c-reduction-in-phase-ii-diabetes-trial.html
A10	FDA Gene Therapy Guidance: Expediting Personalized BLA Approvals	https://www.biospace.com/fda/new-fda-draft-guidance-doubles-down-on-expediting-approvals-of-personalized-gene-therapies
A11	FDA Gene Editing Guidance: BLA Process and IFS for Rare Diseases	https://www.pharmtech.com/view/gene-editing-guidance-shifts-variant-evidence-to-cmc-teams
A12	Sacituzumab Tirumotecan: Survival Gains in Recurrent Endometrial Cancer	https://www.insideprecisionmedicine.com/topics/oncology/trop-2-antibody-drug-conjugate-improves-survival-in-recurrent-endometrial-cancer/
A13	JNJ-6143: Phase 1 results for RIPTAC in advanced prostate cancer	https://www.aol.com/articles/johnson-johnson-reports-75-tumor-073000000.html
A14	MAGEA11-Recruiting PROTACs: Cancer-Selective BET Degradation	https://doi.org/10.1038/s44386-026-00081-2
A15	CB1R Molecular Glue Degraders: Cancer Therapy Strategy for 2026	https://doi.org/10.1038/s44386-026-00087-w

DrugDiscovery_DDS — Selected Articles

Date: 2026-10-31

Articles: 15

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#04 CAMOLE-1: ML-driven discovery of selective MMP12 inhibitors

#05 ZW191 Phase 1 Data: FRα-Targeting ADC Efficacy in PROC Patients

#06 Amgen Imdelltra: Phase 3 DeLLphi-305 results for ES-SCLC

#07 AZD8205: B7-H4 ADC Phase 1/2a results for solid tumors

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#10 FDA Gene Therapy Guidance: Expediting Personalized BLA Approvals

#11 FDA Gene Editing Guidance: BLA Process and IFS for Rare Diseases

#12 Sacituzumab Tirumotecan: Survival Gains in Recurrent Endometrial Cancer

#13 JNJ-6143: Phase 1 results for RIPTAC in advanced prostate cancer

#14 MAGEA11-Recruiting PROTACs: Cancer-Selective BET Degradation

#15 CB1R Molecular Glue Degraders: Cancer Therapy Strategy for 2026

#01 LNP Morphology: Impact of Shape on mRNA Transfection Performance

Published October 22, 2026 bioRxiv

OVERVIEW

Research indicates that the shape and internal architecture of lipid nanoparticles (LNP) significantly determine the magnitude and duration of mRNA transfection. Non-spherical, vesicular morphologies exhibit substantially higher and more sustained protein expression compared to compact spherical structures.

IN DEPTH

Key Findings

The study demonstrates that LNP shape and internal morphology are functionally relevant design variables that directly influence mRNA loading, cellular uptake, and protein expression. Specifically, non-spherical LNP structures resulted in substantially higher and more sustained protein expression than spherical LNPs. While non-spherical LNPs also showed higher cellular uptake, the researchers noted that this increase was relatively modest and cannot alone explain the significant enhancement in transfection performance.

Technical Details

The researchers found that modulating lipid composition—specifically by increasing DSPC content—drives a structural transition from compact spherical morphologies to vesicular non-spherical morphologies. This transition also altered RNA loading at the single-particle level. These observed trends remained consistent across various LNP formulations utilizing clinically relevant ionizable lipids, including:

- SM-102
- ALC-0315
- DLin-MC3-DMA

Background and Context

Lipid nanoparticles are widely employed for nucleic acid delivery. To date, most optimization efforts in the field have focused on refining formulation features, improving therapeutic efficacy, and enabling extrahepatic targeting. However, particle shape and internal architecture have often been overlooked, despite their critical influence on biodistribution, particle stability, and cellular uptake.

Significance and Outlook

These findings establish that the physical morphology of a nanoparticle is as critical as its chemical composition. By identifying the link between DSPC content, particle shape, and the resulting duration and magnitude of mRNA expression, this research provides a new design variable for the development of next-generation LNPs. Incorporating shape and internal structure into the design process may lead to improved mRNA delivery and enhanced therapeutic outcomes.

Source: https://www.biorxiv.org/content/10.64898/2026.10.18.759824v1

Collected: October 31, 2026 | Automated Research System (AI)

#02 Light-Responsive LNPs: VEGFA Editing for CNV Suppression

Published October 27, 2026 bioRxiv

OVERVIEW

Researchers developed a light-responsive lipid nanoparticle (LNP) platform to deliver Cas9 RNP for the spatially controlled editing of the VEGFA gene. In a rat model of choroidal neovascularisation (CNV), a single intravitreal injection combined with light illumination significantly reduced vascular leakage and structural abnormalities. This approach addresses the safety risks associated with unrestricted VEGFA loss while reducing the treatment burden of repeated injections.

IN DEPTH

Key Findings

The study demonstrates that light-responsive lipid nanoparticles can deliver Cas9/sgRNA ribonucleoprotein (RNP) complexes to enable controlled genome editing of VEGFA. In human retinal pigment epithelial cells, light exposure increased the extent of VEGFA disruption compared to non-illuminated conditions, resulting in a corresponding decrease in VEGFA mRNA and protein expression. In a laser-induced rat CNV model, the combination of a single intravitreal injection and light illumination significantly reduced CNV-associated structural abnormalities and vascular leakage compared to vehicle and non-illuminated controls.

Technical Details

The developed LNP platform exhibits the following specifications:

- Mean hydrodynamic diameter: approximately 130 nm.
- Polydispersity: 0.296.
- sgRNA encapsulation efficiency: 90.33%.

The platform utilizes light illumination as the trigger for the release of the Cas9 RNP complexes. Targeted next-generation sequencing was used to confirm the extent of VEGFA disruption in human cells. Ocular safety assessments indicated no apparent nanoparticle-related structural abnormalities in the retina.

Background and Context

Choroidal neovascularisation (CNV) is a primary cause of irreversible vision loss. Current anti-VEGF therapies typically require repeated intravitreal injections, which increase the cumulative risk and treatment burden for patients. While genome editing offers a potential one-time durable suppression of VEGFA, unrestricted loss of the protein can lead to choriocapillaris atrophy and compromised retinal function, creating a significant safety barrier for clinical translation.

Significance and Outlook

By introducing light-controlled release, this platform allows for spatially controlled genome editing, mitigating the risks of total VEGFA depletion. This research provides a foundation for treating VEGFA-driven macular neovascular disease through a method that balances long-term efficacy with precise safety controls.

Source: https://www.biorxiv.org/content/10.64898/2026.10.24.761602v1

Collected: October 31, 2026 | Automated Research System (AI)

#03 pro-DALAP Platform: Yeast-Based Oral Dual GLP-1/GIP Agonist Evaluation

Published October 24, 2026 medRxiv USA

OVERVIEW

Researchers developed a Saccharomyces cerevisiae-based platform to deliver pro-DALAP, a dual GLP-1/GIP receptor agonist, via oral enteric-coated capsules. While in vitro and rat toxicology studies showed functionality and safety, a 12-week clinical trial in overweight adults did not yield statistically significant differences in body weight or waist circumference compared to dietary guidance.

IN DEPTH

Key Findings

The preliminary clinical evaluation of the pro-DALAP platform showed no statistically significant difference between the intervention group and the control group regarding body weight and waist circumference over 12 weeks. At week 12, the intervention group showed a mean body weight reduction of −0.76% compared to −0.27% in the control group, and a waist circumference reduction of −3.60% versus −3.69% for the control. An interim week-8 analysis of eight participants per group had shown numerically greater reductions in body weight (−2.29% vs. +0.14%) and waist circumference (−6.34% vs. −2.32%), but these trends were not reproduced in the final analysis. HbA1c reduction favored the control group, while 37 of 40 survey respondents in the intervention group reported no side effects.

Technical Details

The platform utilizes a protease-deficient yeast strain engineered via CRISPR/Cas12a to integrate three expression cassettes. This process yielded 4.05 ± 0.31 mg pro-DALAP/g dry biomass, significantly higher than the 1.27 ± 0.21 mg/g produced by the single-copy strain. The pro-DALAP fusion precursor is engineered with several components to overcome intestinal permeability and enzymatic degradation:

- Maltose-binding protein and a GM1-binding peptide for epithelial uptake.
- A cell-penetrating peptide and an albumin-binding domain for stability and prolonged systemic exposure.
- Furin cleavage sites for proteolytic activation.

In vitro assays confirmed GM1 binding, furin-mediated processing, and activation of both GLP-1 and GIP receptors.

Background & Context

The study addresses the limitations of oral delivery for biologics, specifically enzymatic degradation and poor permeability. To test the platform, a 12-week, open-label, randomized controlled trial was conducted with 98 generally healthy, overweight adults. The intervention consisted of enteric-coated capsules containing lyophilized yeast expressing pro-DALAP. Additionally, intravenous toxicology studies in rats showed no treatment-related adverse findings at doses up to 300 µg/kg/day for seven days.

Significance & Outlook

The results validate the yeast-based production and in vitro functionality of pro-DALAP. However, the lack of statistical significance in the clinical trial indicates that further research is required. The authors state that validated pharmacokinetic measurements and adequately powered, blinded, placebo-controlled trials with longer follow-up periods are necessary to determine systemic exposure and evaluate sustained benefits.

Source: https://www.medrxiv.org/content/10.64898/2026.10.22.26365662v1

#04 CAMOLE-1: ML-driven discovery of selective MMP12 inhibitors

Published October 26, 2026 bioRxiv USA

OVERVIEW

Calico Life Sciences developed CAMOLE-1, a machine learning platform that utilizes an all-atom diffusion model to design potent and selective peptide inhibitors. The system successfully optimized an MMP12 inhibitor over approximately one year through the synthesis of 270 peptides. This approach demonstrates the ability of ML to drive peptide design from initial hit discovery to lead development with improved pharmacokinetic properties.

IN DEPTH

Key Findings

The CAMOLE-1 platform enabled the discovery and optimization of a potent and selective inhibitor for matrix metalloproteinase 12 (MMP12). By integrating an all-atom diffusion model with physics-based computational filtering and biochemical testing, the researchers developed a lead peptide inhibitor within approximately one year, synthesizing a total of 270 peptides during the process.

Technical Details

CAMOLE-1 is a de novo peptide inhibitor design platform. Its core technical components include:

- **All-atom diffusion model:** This enables the rapid discovery and optimization of non-canonical peptides.
- **Iterative Workflow:** The process began with canonical amino acid-based designs to identify an initial MMP12 peptide inhibitor, which was then further optimized for potency.
- **Structural Validation:** Predicted structures for both canonical and non-canonical peptide inhibitors showed high fidelity when compared to experimentally determined peptide-bound crystal structures.
- **Integrated Filtering:** The platform combines machine learning with physics-based computational filtering and biochemical testing to refine candidates.

Background & Context

Peptide therapeutics are an emerging modality offering increased potency and reduced toxicity compared to other options. The researchers targeted matrix metalloproteinases (MMPs), a class of targets that has essentially evaded therapeutic development until now. This work represents the first described effort to use machine learning techniques to iteratively drive peptide inhibitor design beyond the initial hit discovery phase into the development of selective, potent lead inhibitors.

Significance & Outlook

The successful application of CAMOLE-1 illustrates the potential of machine learning to accelerate drug discovery pipelines for complex targets. By improving pharmacokinetic properties and achieving high selectivity, the study highlights the power of ML-driven design in the emerging field of peptide therapeutics.

Source: https://www.biorxiv.org/content/10.64898/2026.10.21.755545v1

Collected: October 31, 2026 | Automated Research System (AI)

#05 ZW191 Phase 1 Data: FRα-Targeting ADC Efficacy in PROC Patients

Published October 26, 2026 BioSpace Canada

OVERVIEW

Zymeworks presented Phase 1 data for ZW191, showing a 64.5% confirmed objective response rate (cORR) at the 6.4 mg/kg dose in patients with high-grade serous platinum-resistant ovarian cancer (PROC). The ADC demonstrated anti-tumor activity across all folate receptor alpha (FRα) expression levels, including low or negative expression. These results suggest a potential for broader patient eligibility compared to existing FRα-targeted therapies.

IN DEPTH

Key Findings

At the ESMO Congress 2026, Zymeworks reported that ZW191 achieved a confirmed objective response rate (cORR) of 64.5% at the 6.4 mg/kg dose and 55.3% at the 9.6 mg/kg dose in patients with high-grade serous PROC. Disease control rates were 100% and 92.1%, respectively. Notably, the drug showed activity regardless of FRα expression levels: cORR was 69.2% in high expression, 50.0% in intermediate expression, and 55.0% in low or negative expression patients.

Technical Details

The randomized dose-optimization study included 80 heavily pretreated PROC patients (median of four prior lines of therapy; 45% receiving five or more). Patients were randomized to receive ZW191 at either 6.4 mg/kg (n=37) or 9.6 mg/kg (n=43) every three weeks. FRα expression was categorized via immunohistochemistry as low/negative (0%–24%), intermediate (25%–74%), or high (75%–100%).

Regarding durability, the median duration of response was not yet reached at either dose level at a median follow-up of seven months. The six-month progression-free survival (PFS) rate was 61% for both groups, with median PFS reaching 7.9 months at 6.4 mg/kg and 9.8 months at 9.6 mg/kg in high-grade serous PROC patients.

Safety and Tolerability

The 6.4 mg/kg dose exhibited a more favorable safety profile. Grade 3 or higher treatment-related adverse events occurred in 22% of patients at 6.4 mg/kg, compared to 44% at 9.6 mg/kg. Dose reductions due to treatment-emergent adverse events were reported in 5% of the 6.4 mg/kg group and 33% of the 9.6 mg/kg group. Discontinuations due to adverse events were 14% and 19%, respectively. No treatment-related deaths were reported.

Significance and Outlook

The data indicates that ZW191 may address limitations of current FRα-targeted therapies by providing meaningful benefit to patients with lower FRα expression who are typically ineligible for existing treatments. Zymeworks intends to use these results to guide dose selection for the next stage of clinical development, potentially through a strategic collaboration or partnership.

Source: https://www.biospace.com/press-releases/zymeworks-presents-new-phase-1-data-for-folate-receptor-alpha-targeting-antibody-drug-conjugate-zw191-at-esmo-congress-2026

#06 Amgen Imdelltra: Phase 3 DeLLphi-305 results for ES-SCLC

Published October 26, 2026 BioSpace USA

OVERVIEW

Amgen's Imdelltra, combined with AstraZeneca's Imfinzi, reduced the risk of death by 58% compared to Imfinzi alone in first-line maintenance treatment for extensive-stage small cell lung cancer (ES-SCLC). The combination extended median overall survival to 21.1 months, potentially expanding the drug's U.S. addressable patient population to approximately 21,600.

IN DEPTH

Key Findings

In the Phase 3 DeLLphi-305 study, the combination of Imdelltra and Imfinzi significantly improved survival outcomes for patients with extensive-stage small cell lung cancer (ES-SCLC). At a median follow-up of 16 months, the combination therapy reduced the risk of death by 58% compared to Imfinzi alone. Median overall survival (OS) was 21.1 months for the combination group versus 12.7 months for the monotherapy group.

Regarding disease progression, the combination lowered the risk of progression or death by 66% at a median follow-up of 13.9 months. Median progression-free survival (PFS) was 7.4 months for the combination versus 1.9 months for Imfinzi alone.

Technical Details

Imdelltra is a bispecific T cell engager targeting DLL3 and CD3 proteins to activate T cells against cancer cells. The DeLLphi-305 trial enrolled 563 ES-SCLC patients who had completed prior treatment with Imfinzi, platinum chemotherapy, and etoposide without disease progression. Results were presented at the ESMO Congress 2026 and published in The New England Journal of Medicine.

Safety data showed that 20.9% of patients in the combination arm experienced severe or medically significant treatment-emergent adverse events, compared to 10.8% in the Imfinzi arm. Nearly half of Imdelltra patients experienced cytokine release syndrome, though most cases were mild or moderate, and no deaths were reported.

Background and Context

Imdelltra was first approved in May 2024 for ES-SCLC, but its current label is limited to patients whose cancer progressed after platinum-based chemotherapy. Expanding into the first-line maintenance setting would increase the U.S. addressable market from 12,900 patients to approximately 21,600 patients.

Significance and Outlook

Amgen intends to submit these findings to global regulatory authorities with urgency. Beyond first-line ES-SCLC, Amgen is exploring combinations with antibody-drug conjugates (ADCs) in the DeLLphi-310 study (with YL201) and the DeLLphi-313 trial (with ZL-1310). Future development plans include testing Imdelltra in neuroendocrine carcinomas, melanoma, certain gliomas, and pediatric neuroblastomas.

Source: https://www.biospace.com/drug-development/esmo-2026-amgens-imdelltra-slashes-death-risk-by-nearly-60-in-small-cell-lung-cancer

Collected: October 31, 2026 | Automated Research System (AI)

#07 AZD8205: B7-H4 ADC Phase 1/2a results for solid tumors

Published October 30, 2026 BIOENGINEER.ORG USA

OVERVIEW

The first-in-human BLUESTAR trial of the B7-H4-directed antibody-drug conjugate AZD8205 (puxitatug samrotecan) demonstrated partial tumor responses in patients with advanced ovarian, endometrial, and breast cancers. With an objective response rate of 20.5% in the efficacious exposure group, the study establishes clinical proof of concept for B7-H4 as a viable ADC target.

IN DEPTH

Key Findings

The Phase 1/2a BLUESTAR study reported that AZD8205 induced partial responses in patients with advanced or metastatic ovarian, endometrial, and breast cancers. Among the 44 patients treated at doses of 1.6 milligrams per kilogram or higher—the predicted efficacious exposure range—the objective response rate was 20.5%, with 9 patients achieving a partial response. The trial included 47 patients with B7-H4-positive solid tumors who had previously undergone treatment.

Technical Details

AZD8205, also known as puxitatug samrotecan, is an antibody-drug conjugate that pairs a B7-H4-directed antibody with a topoisomerase-1 inhibitor payload via a stable cleavable linker. This architecture enables the release of the cytotoxic payload within B7-H4-expressing cells and provides a bystander effect on adjacent tumor cells. In the trial, the drug was administered intravenously every three weeks at doses between 0.8 and 3.2 milligrams per kilogram.

Safety data indicated that the most frequent treatment-related adverse events were nausea (51.1%), neutropenia (48.9%), and anemia (38.3%). Dose-limiting neutropenia and thrombocytopenia were observed at the highest dose of 3.2 milligrams per kilogram, defining the upper limit of tolerability.

Background and Context

B7-H4 is a protein highly expressed in various solid tumors but limited in normal tissue. It contributes to tumor progression by negatively regulating T-cell function, making it a strategic target for targeted therapy. Translational analyses from the trial confirmed the selective localization of the topoisomerase-1 inhibitor to B7-H4-expressing cells and the subsequent induction of target-dependent DNA damage.

Significance and Outlook

These results provide the first clinical proof of concept for B7-H4 as an ADC target. The response signals are particularly significant given that the study population consisted of heavily pretreated patients. While the trial was primarily designed for safety and dose identification rather than definitive efficacy, the manageable toxicity profile and mechanistic evidence support further development to refine dosing and expand testing across other B7-H4-positive malignancies.

Source: https://bioengineer.org/first-in-human-trial-shows-b7-h4-antibody-drug-conjugate-shrinks-ovarian-endometrial-and-breast-tumors/

Collected: October 31, 2026 | Automated Research System (AI)

#08 XmAb819: Phase 1 Dose Selection and ccRCC Development Roadmap

Published October 25, 2026 Yahoo Finance (Business Wire) USA

OVERVIEW

Xencor has selected 400 mcg/kg as the proposed IV recommended Phase 3 dose (RP3D) for XmAb819, showing a 45.5% cORR and 82% 6-month PFS estimate. The company plans to discuss an accelerated FDA approval pathway in 1H2027 for specific advanced clear cell renal cell carcinoma (ccRCC) subgroups.

IN DEPTH

Key Findings

Xencor presented updated Phase 1 data for XmAb819, a potential first-in-class ENPP3 x CD3 bispecific T-cell engager, at the ESMO Congress 2026. The company identified 400 mcg/kg as the proposed intravenous RP3D based on a confirmed objective response rate (cORR) of 45.5%, an unconfirmed objective response rate (uORR) of 55%, and a 6-month PFS Kaplan-Meier estimate of 82%.

Technical Details

The Phase 1 study enrolled 119 patients with advanced ccRCC across 11 IV target dose levels, utilizing a weekly priming regimen followed by a maintenance dose. Expansion cohorts (n=68) evaluated three dose levels: 100 mcg/kg, 200 mcg/kg, and 400 mcg/kg. The patient population was heavily pre-treated, with a median of three prior lines of therapy; 94% were intermediate- to poor-risk per the IMDC model. All patients had prior exposure to at least one PD-(L)1 inhibitor and one VEGFR TKI, with 63% having received two or more VEGFR TKIs and 34% having received at least one HIF2α inhibitor.

Of the 25 patients with confirmed responses per RECIST v1.1, one achieved a complete response and 24 achieved partial responses. As of the September 1, 2026 data-cut, 19 responses remained ongoing with a median treatment time of 7 months.

Safety data showed a 5.9% treatment discontinuation rate due to treatment-emergent adverse events (TEAEs). Grade 3 or higher related TEAEs occurred in 72.1% of patients, most commonly liver enzyme elevations (AST increased: 35.3%; ALT increased: 33.8%), rash (22.1%), hypotension (7.4%), and cytokine release syndrome (5.9%).

Background & Context

XmAb819 is an engineered XmAb 2+1 bispecific antibody designed to selectively target malignant cells in solid tumors. It offers a distinct mechanism of action compared to current ccRCC treatments, which primarily rely on checkpoint inhibitors and VEGF-axis targeted therapies.

Significance & Outlook

Xencor intends to initiate a registration-enabling study by the end of 2027. This includes a global randomized study comparing XmAb819 monotherapy against tivozanib in ccRCC patients who have progressed after PD-(L)1 and VEGFR TKI therapy. The company maintains a cash runway into 2029 to support clinical development in oncology and autoimmune diseases.

Source: https://finance.yahoo.com/healthcare/articles/xencor-presents-phase-1-dose-083500804.html

Collected: October 31, 2026 | Automated Research System (AI)

#09 Ascletis ASC30: Phase II Results for Oral GLP-1 in Type 2 Diabetes

Published October 30, 2026 BioPharma APAC China

OVERVIEW

Ascletis Pharma's oral small molecule GLP-1 receptor agonist, ASC30, achieved a placebo-adjusted HbA1c reduction of up to 1.7% and weight loss of up to 4.4% in a U.S. Phase II trial for type 2 diabetes. The drug demonstrated favorable gastrointestinal tolerability with zero discontinuations due to GI adverse events. These results position ASC30 as a potential once-daily oral treatment for both diabetes and obesity.

IN DEPTH

Key Findings

In a 13-week U.S. Phase II study (NCT07321678) involving 100 participants with type 2 diabetes (T2D), ASC30 met its primary and all secondary endpoints. The primary endpoint, HbA1c reduction at 12 weeks, showed placebo-adjusted decreases of 1.7% for the 40 mg dose, 1.6% for 60 mg, and 1.7% for 80 mg ($p < 0.0001$). Baseline HbA1c for participants averaged 8.3%.

Regarding the secondary endpoint of body weight reduction at 13 weeks, ASC30 achieved placebo-adjusted reductions of 4.4%, 3.8%, and 4.0% for the 40 mg, 60 mg, and 80 mg doses, respectively ($p = 0.001$ to 0.003). No weight loss plateau was observed during the study period; baseline average body weight was 93.7 kg.

Technical Details and Safety

ASC30 is an investigational small molecule GLP-1R fully biased agonist administered as a once-daily tablet. Despite a fast weekly titration to maintenance doses, the drug showed favorable safety and gastrointestinal (GI) tolerability. There were zero study discontinuations due to GI adverse events, and only one total discontinuation (1.3%) due to a hiccup. All drug-related adverse events were categorized as grade 1 (mild) or grade 2 (moderate), with no drug-related serious adverse events (SAEs) reported.

Hepatic safety signals were absent, with no elevations observed in alanine transaminase (ALT), aspartate aminotransferase (AST), or total bilirubin (TBL). Ascletis expects GI tolerability to improve further in Phase III trials by slowing titration to once every four weeks.

Background and Outlook

T2D is the second indication for ASC30, following obesity. The company is currently conducting a global Phase III program for obesity (AURORA-1 and AURORA-2) in the U.S., Europe, and Canada, enrolling approximately 4,600 participants. Topline data for the obesity program are expected in Q3 2028, with an FDA New Drug Application (NDA) submission planned for late 2028 and an EMA Marketing Authorisation Application (MAA) expected in early 2029. If approved, ASC30 could become the second oral small molecule GLP-1 receptor agonist available in these markets.

Source: https://biopharmaapac.com/news/31/8617/ascletis-oral-glp-1-asc30-delivers-up-to-1-7-hba1c-reduction-in-phase-ii-diabetes-trial.html

#10 FDA Gene Therapy Guidance: Expediting Personalized BLA Approvals

Published October 28, 2026 BioSpace USA

OVERVIEW

The FDA and CMS have introduced a draft guidance allowing a single Biologics License Application (BLA) to cover multiple personalized gene therapy variants. This framework, combined with the expansion of the CMS Cell and Gene Therapy Access Model, aims to accelerate patient access to treatments for ultra-rare diseases.

IN DEPTH

Key Findings

The FDA has issued draft guidance designed to accelerate the approval process for personalized gene therapies. The central objective is to allow a single BLA to encompass multiple product variants, reducing the need for additional clinical trials when new patient-specific variants are developed. Simultaneously, the Centers for Medicare & Medicaid Services (CMS) is expanding its Cell and Gene Therapy (CGT) Access Model to improve patient access to these high-cost therapies.

Technical Details

The guidance introduces the Individualized Feature Space (IFS), a framework of pre-defined criteria that defines how a gene therapy can vary between patients—such as those with different genetic mutations—while remaining within the scope of one BLA. Under this system, if a new patient-specific variant falls within the IFS boundaries and assays confirm adequate safety and activity, sponsors can add the variant to the BLA without performing new clinical trials. The document also provides specifications for manufacturing, safety testing, and labeling for these multi-variant applications.

Background and Context

This initiative follows the "Plausible Mechanism Pathway" announced in November last year by former Commissioner Marty Makary and former CBER director Vinay Prasad, which targets diseases where randomized trials are not feasible. A case study published in The New England Journal of Medicine on Nov. 13, 2025, highlighted "Baby KJ," a child with CPS1 deficiency treated with a single-use CRISPR therapy, as an example of this pathway's intent. Additionally, the FDA recently debuted the Rare Disease Framework Initiative to standardize scientific evidence requirements.

Significance and Outlook

To address affordability, CMS Administrator Mehmet Oz stated that CMS is coordinating state Medicaid programs to negotiate with manufacturers. The CGT Access Model, which initially focused on sickle cell disease and included Vertex Pharmaceuticals and bluebird bio (developers of Casgevy and Lyfgenia), will be broadened. CMS will soon release a Request for Applications (RFA) to allow negotiations to begin sooner after FDA licensure. RBC Capital Markets analysts noted a constructive tone from CBER and CDER leadership regarding the harmonization of regulatory standards to increase predictability for sponsors.

Source: https://www.biospace.com/fda/new-fda-draft-guidance-doubles-down-on-expediting-approvals-of-personalized-gene-therapies

#11 FDA Gene Editing Guidance: BLA Process and IFS for Rare Diseases

Published October 28, 2026 Pharmaceutical Technology (PharmTech) USA

OVERVIEW

The FDA has issued draft guidance allowing biologics license applications (BLAs) for individualized genome editing products to add patient-specific variants without new clinical trials. By shifting the evidentiary burden to CMC assay data and the "Individualized Feature Space" (IFS), the framework accelerates access to therapies for ultrarare genetic diseases.

IN DEPTH

Key Findings

On October 27, 2026, the FDA released draft guidance titled “Individualized Human Genome Editing Products: Considerations for BLA Submission and Postapproval Management.” The guidance establishes a mechanism where a single BLA can cover therapies that vary by patient. If a new patient-specific variant falls within a predefined Individualized Feature Space (IFS) and demonstrates adequate safety and activity via assays, it can be added to the BLA through a streamlined review process based on original clinical trials and in vitro data.

Technical Details

The IFS defines the boundaries within which a product may vary while remaining under one license. This shift moves the regulatory burden from clinical data to analytical and process data. Critical technical requirements include:

- **CMC Evidence:** High regulatory weight is placed on assays characterizing on-target editing and off-target activity, as well as platform process consistency.
- **Off-Target Assessment:** Per April 2026 guidance, safety assessments should use the final product's editor, cells representative of target tissue, and on-target editing rates comparable to the drug product.
- **Data Submission:** Sponsors may be required to submit raw sequencing data and analysis scripts.

Background & Context

This framework builds on the Plausible Mechanism Framework, allowing variants targeting mutations not studied in initial trials to be added if the mechanism of action is well-supported. It also aligns with the FDA’s Rare Disease Framework Initiative, which incorporates risk-based CMC review and preapproval inspections. Simultaneously, the CMS is expanding its Cell and Gene Therapy Access Model beyond sickle cell disease, negotiating outcomes-based agreements with manufacturers to reduce administrative burdens for state Medicaid programs.

Significance & Outlook

The guidance transforms the definition of IFS boundaries into a critical CMC decision. Narrow boundaries limit the patient population per license, while overly broad boundaries may lack sufficient characterization data. This regulatory shift is intended to provide more efficient access to life-changing therapies for patients with ultrarare conditions.

Source: https://www.pharmtech.com/view/gene-editing-guidance-shifts-variant-evidence-to-cmc-teams

Collected: October 31, 2026 | Automated Research System (AI)

#12 Sacituzumab Tirumotecan: Survival Gains in Recurrent Endometrial Cancer

Published October 26, 2026 Inside Precision Medicine USA

OVERVIEW

Sacituzumab tirumotecan (sac-TMT) significantly extended overall survival to 19.0 months compared to 12.1 months for conventional chemotherapy in patients with advanced or recurrent endometrial cancer. This Phase III trial demonstrates a new treatment option for patients who have already progressed on platinum-based chemotherapy and immunotherapy.

IN DEPTH

Key Findings

The Phase III TroFuse-005 trial demonstrated that sacituzumab tirumotecan (sac-TMT) significantly improves survival and tumor response rates in women with advanced or recurrent endometrial cancer. Median overall survival reached 19.0 months with sac-TMT, compared to 12.1 months with physician-selected chemotherapy (doxorubicin or paclitaxel), representing a 32% reduction in the relative risk of death. Median progression-free survival increased from 3.9 to 7.2 months, a 41% reduction in the risk of progression or death. The tumor response rate was 35.1% for sac-TMT versus 17.3% for chemotherapy, with a longer median response duration of 11.1 months compared to 6.9 months.

Technical Details

Sac-TMT is an antibody-drug conjugate (ADC) that targets TROP2, a protein frequently overexpressed on endometrial cancer cells. The drug utilizes an engineered linker to deliver a potent cytotoxic payload directly to tumor cells, aiming to increase antitumor activity while limiting systemic exposure. The international trial involved 776 patients across more than 200 cancer centers in 29 countries. All participants had previously received anti-PD-1/PD-L1 immunotherapy and platinum-based chemotherapy.

Background and Context

Endometrial cancer is the most common gynecologic cancer in the United States, with projected figures for 2026 showing approximately 68,000 new cases and over 14,000 deaths. While frontline therapies have advanced with the use of pembrolizumab or dostarlimab alongside platinum-based chemotherapy, and pembrolizumab combined with lenvatinib for certain patients, effective options remain limited after these regimens fail.

Significance and Outlook

While sac-TMT showed superior efficacy, it was associated with higher toxicity; severe treatment-related adverse events occurred in 54.4% of recipients versus 41.4% in the chemotherapy group. The most common severe complication was anemia, with other effects including neutropenia, mouth inflammation, and dry or itchy eyes. Despite this, fewer patients discontinued sac-TMT due to adverse events. Researchers concluded that the drug provides clinically meaningful improvements in survival with manageable safety.

Source: https://www.insideprecisionmedicine.com/topics/oncology/trop-2-antibody-drug-conjugate-improves-survival-in-recurrent-endometrial-cancer/

Collected: October 31, 2026 | Automated Research System (AI)

#13 JNJ-6143: Phase 1 results for RIPTAC in advanced prostate cancer

Published October 25, 2026　AOL (J&Jプレスリリース)　USA

OVERVIEW

Johnson & Johnson reported a 75% complete or partial tumor response rate in patients with advanced prostate cancer treated with JNJ-6143. The once-daily oral molecule demonstrated significant PSA reductions in patients who had failed multiple prior therapies. These results support the advancement of the 50-mg dose into Phase 2 clinical trials.

IN DEPTH

Key Findings

In a Phase 1 study of JNJ-6143, 75% (12 out of 16) of patients with measurable disease achieved a confirmed complete or partial response based on RECIST criteria. Among 38 patients receiving the 50-mg once-daily dose, 77% achieved a confirmed reduction in prostate-specific antigen (PSA) levels of at least 50%, with 48% seeing reductions of at least 90%. At the time of analysis, 71% of patients in the 50-mg cohort remained on treatment with a median follow-up of 5.6 months.

Technical Details

JNJ-6143 (formerly HLD-0915) is the first molecule from Johnson & Johnson's Regulated Induced Proximity Targeting Chimera (RIPTAC) platform to enter clinical studies. It is a novel, once-daily oral small molecule designed to trigger cancer cell death via a targeted dual-protein lock. This mechanism links the androgen receptor (AR)—a tumor-selective protein highly expressed in prostate cancer cells—with BRD4, an essential cell survival protein, thereby disrupting cancer cell function.

Background and Context

The study targeted patients with advanced prostate cancer who had received a median of four prior therapies, including chemotherapy and PSMA-targeted radioligand therapy. This population includes those with metastatic androgen pathway modulation-resistant prostate cancer (mAPMR), also known as metastatic castration-resistant prostate cancer (mCRPC), where median overall survival is approximately two to three years. The Phase 1 trial (NCT06800313) was designed to evaluate safety and anti-tumor activity to identify the optimal dose for further development.

Significance and Outlook

The most common treatment-related adverse events were elevated cholesterol (18%), nausea (16%), and elevated triglyceride levels (16%). Adverse events led to dose interruption in 11% of patients, dose reduction in 3%, and discontinuation in 3%. Based on these data, the 50-mg once-daily dose will proceed to a Phase 2 study (NCT07832292) in metastatic prostate cancer. The company intends to further explore the RIPTAC platform across various other cancer types.

Source: https://www.aol.com/articles/johnson-johnson-reports-75-tumor-073000000.html

Collected: October 31, 2026 | Automated Research System (AI)

#14 MAGEA11-Recruiting PROTACs: Cancer-Selective BET Degradation

Published October 26, 2026 npj Drug Discovery (Europe PMC記録)

OVERVIEW

Researchers have developed the first PROTAC that recruits the tissue-specific E3 ligase scaffolding protein MAGEA11 to achieve cancer-restricted protein degradation. Lead compound 105B degrades BET proteins in osteosarcoma and esophageal squamous cell carcinoma cells while showing no degradation in non-cancerous HEK293T cells. This approach provides a strategy to increase the therapeutic window by targeting E3 ligases overexpressed in specific tissues.

IN DEPTH

Key Findings

The study identifies lead compound 105B, a PROTAC designed to recruit the tissue-specific E3 ligase scaffolding protein MAGEA11 for the degradation of bromodomain and extra-terminal domain (BET) proteins. In osteosarcoma U2OS cells, 105B demonstrated a BRD4 DC50 of 0.130 nM and a Dmax of 78%. In KYSE180 esophageal squamous cell carcinoma cell lines, the compound showed a DC50 of 40 nM and a Dmax of 70%. Notably, no degradation was observed in non-cancerous HEK293T cells. Mechanistic analysis confirmed that 105B depends on MAGEA11 and HUWE1 expression, as well as the ubiquitin-proteasome system.

Technical Details

PROTACs are heterobifunctional molecules that link a ligand for a protein of interest (POI) to a ligand for an E3 ligase. This creates a ternary complex that allows the E3 ligase to transfer ubiquitin to the POI, leading to proteasome-mediated degradation. While most PROTACs utilize ubiquitously expressed E3 ligases like cereblon or von Hippel-Lindau (VHL), this design recruits MAGEA11. MAGEA11 binds to the E3 ligase HUWE1 to direct ubiquitination. The lead compound 105B successfully decreased levels of BET-regulated gene products RUNX2 and KRT14, though the authors note that further improvements are required to affect selective cytotoxicity.

Background & Context

BET proteins, including BRD4, are epigenetic readers that regulate gene transcription by binding to acetylated lysine residues on histones. Due to their role in tumorigenesis, they are primary targets for degradation, though their inhibition is often associated with dose-limiting toxicities. MAGEA11 is a cancer-testis antigen expressed in sperm and placental tissues in healthy individuals, but it is aberrantly expressed in various cancers, including non-small cell lung carcinoma, castration-resistant prostate carcinoma, osteosarcoma, and esophageal squamous cell carcinoma.

Significance & Outlook

By recruiting a tissue-specific E3 ligase rather than a ubiquitous one, this method increases the specificity of protein degradation. This reduces the risk of off-target effects in healthy tissues, similar to how VHL-based PROTACs targeting BCL-xL show limited degradation in platelet cells to reduce thrombocytopenia. This work establishes the feasibility of MAGEA11-recruiting degraders for cancer-restricted therapy.

Source: https://doi.org/10.1038/s44386-026-00081-2

Collected: October 31, 2026 | Automated Research System (AI)

#15 CB1R Molecular Glue Degraders: Cancer Therapy Strategy for 2026

Published October 26, 2026 npj Drug Discovery (Europe PMC記録)

OVERVIEW

Researchers have developed covalent molecular glue degraders, specifically MG-CB2, to reduce the abundance of cannabinoid receptor type 1 (CB1R) in cancer cells. The approach targets the ubiquitin-proteasome system to inhibit oncogenic signaling and reduce cell viability in breast and hepatocellular carcinoma.

IN DEPTH

Key Findings

The study identifies MG-CB2 as the most active covalent molecular glue degrader designed to reduce the abundance of the G protein-coupled receptor CB1R. In MCF-7 breast cancer and HepG2 hepatocellular carcinoma cells, MG-CB2 induced the depletion of CB1R in a concentration- and time-dependent manner. This degradation resulted in reduced cancer-cell viability and migration.

Technical Details

The degraders were developed using rimonabant as a CB1R-binding scaffold, incorporating electrophilic E3 ligase-recruiting handles. The mechanism of action is dependent on the proteasome and the E3 ligase RNF126, as proteasome inhibition and RNF126 knockdown both blocked the loss of CB1R. Cellular engagement was confirmed via rimonabant competition and cellular thermal shift experiments.

Degradation of CB1R led to the modulation of associated signaling pathways, specifically:

- Reduced phosphorylation of ERK and mTOR.
- Decreased expression of the anti-apoptotic protein BCL2.

Background & Context

CB1R is a major regulatory element of the endocannabinoid system, expressed in the central nervous system and peripheral organs including the liver and skeletal muscle. While it regulates mood, appetite, and motor activity, aberrant CB1R signaling is linked to chronic liver disease and cancer. In breast cancer and hepatocellular carcinoma, CB1R upregulation is associated with increased tumor aggressiveness. This occurs because CB1R activates the ERK and mTOR pathways and upregulates BCL2, creating a pro-survival network that inhibits apoptosis and promotes proliferation.

Significance & Outlook

Traditional pharmacological modulators of CB1R are limited to agonists (e.g., THC) or antagonists/inverse agonists (e.g., rimonabant). The development of MG-CB2 demonstrates that covalent molecular glue-mediated degradation can effectively modulate the abundance of a transmembrane GPCR. This establishes a new strategy for targeting disease-associated proteins that were previously managed only through signaling inhibition.

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