EDITION 056

WEDNESDAY, NOVEMBER 25, 2026

MIND CLUB

Biotech & Pharma

Intelligence

BIOTECH SIGNAL · PDMC.BIO

SPECIAL COVERAGE · THE EDITION IN FOUR SQUARES

04S · P. 09

The biggest I&I deal in our count

DATA

01 · P. 07

FDA approved Cogent's Ekitna (bezuclastinib) with sunitinib for advanced GIST after imatinib

GOV

02 · P. 08

CMS proposed its 2028 Medicare Advantage and Part D rule; comments close 01.19.2027

GOV

03 · P. 08

PITSTOP: antibiotics or extra fluids in the ambulance did not lower sepsis deaths

PEER

THE OPEN QUESTION · P. 03

Does Ekitna's progression-free gain carry to overall survival? It was not mature at approval; later PEAK analyses should settle it.

THIS EDITION

Insmed, $41.0B: largest of 26 I&I deals since 2019

SCIENCE

SANOFI'S $41.0 BILLION INSMED OFFER IS THE LARGEST I&I ACQUISITION IN OUR COUNT SINCE 2019. FDA APPROVED EKITNA FOR ADVANCED GIST SIX DAYS EARLY.

Special Coverage: Sanofi, Insmed and the I&I deal market. FDA approved Cogent's Ekitna with sunitinib for advanced GIST. Two JAMA trials found no survival gain from antibiotics or extra fluids in the ambulance for sepsis.

XBI · 11.24	IBB · 11.24	UST 10-YEAR	US BIOTECH IPOS YTD
156.82	**219.49**	**4.91%**	**30**
1D +6.6% · 1W +7.9% 1M +4.9% · YTD +28.6%	1D +5.2% · 1W +6.1% 1M +5.7% · YTD +30.1%	11.24 · −1BP FROM 11.23 2Y 4.63% · 2S10S +28BP	~$8.2B RAISED MIND CLUB TALLY · 11.25

Market figures as of the 11.24 close: XBI and IBB from Robinhood market data (price returns: 1D vs 11.23, 1W vs 11.17, 1M vs 10.23, YTD vs 12.31.2025); yields from the U.S. Treasury daily par yield curve (11.24); IPOs from the Mind Club financing tally (US biotech IPOs in the Mind Club tally, $5M or more, 11.25). SPY, IWM, fed funds and the VIX print in 01 Markets & outlook. Facts only, not a view on any security.

VERIFICATION AT A GLANCE

CLAIM CHECK	CALENDAR DATES	REGISTRY WATCH	OPEN CALLS	CORRECTIONS
5	**6/7**	**70**	**10**	**19**
2 match · 2 partial · 1 open	confirmed at the source	trials · 1 change · see 14B	10 new today · see 15	2 new · see 16

THE FIVE-MINUTE READ

THREE THAT MATTER · ONE DESK · ONE DATE · ONE OPEN QUESTION

#	WHAT HAPPENED	SO WHAT · OUR ANALYSIS	PRIORITY · SOURCES	PAGE
SPECIAL	**Special Coverage: Sanofi, Insmed and the I&I deal market.** Sanofi's $41.0 billion cash offer for Insmed is the largest acquisition in immunology and inflammation in our count of 26 such deals since 2019. Our ledger, the comparison with oncology, what buyers paid for, China, and the 2027 dates.			09
01	**FDA approved Cogent's Ekitna (bezuclastinib) with sunitinib for advanced GIST after imatinib, six days before its goal date.** In PEAK (413 patients), median progression-free survival was 16.5 vs 9.2 months on sunitinib alone.	The combination adds a selective KIT inhibitor to sunitinib, the trial's comparator. Overall survival was not mature at approval, and the label carries a boxed warning for liver toxicity.	MUST READ GOV CO	07
02	**CMS proposed its 2028 Medicare Advantage and Part D rule.** It covers drug coverage, marketing and enrollment, and a mandatory Innovation Center model; comments close 01.19.2027.	Part D coverage terms for 2028 are open for comment. We have read the abstract only.	KNOW IT GOV	08
03	**Antibiotics or extra fluids in the ambulance did not lower sepsis deaths in PITSTOP (JAMA).** Hospital mortality was 18.0% vs 18.4% for ceftriaxone vs placebo.	A large randomized test of earlier antibiotics found no survival gain; the intervals still allow a modest effect either way.	KNOW IT PEER REG	08

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#		WHAT HAPPENED	SO WHAT · OUR ANALYSIS	PRIORITY · SOURCES	PAGE
	+	**Also today.** 04 DiaMedica priced an $86 million offering, with a top five pharma company among the buyers, per the company. 05 Amgen settled its Opdivo biosimilar patent case, with a U.S. launch set for 10.01.2028, subject to FDA approval.			09
	DATE	**One date to hold.** Mon 11.30: FDA goal date for Vertex's povetacicept in IgA nephropathy, per Vertex; no action found as of 11.25.			32
	OPEN	**The open question.** Does Ekitna's progression-free gain carry to overall survival? It was not mature at approval; later PEAK analyses should settle it.			31

HOW TO READ THIS BRIEF

MUST READ understand today. KNOW IT secondary. SCAN awareness only. VERIFIED a primary source was checked, CLAIM a company statement, ANALYSIS our interpretation, FORECAST a dated judgment with odds. Red boxes are the red team.

Source badges: REG trial registry GOV agency or government PEER peer-reviewed journal PRE preprint CO company or organizer release or filing DATA curated database PRESS journalism.

Claim Check verdicts compare a headline with the registered protocol: MATCH PARTIAL MISMATCH OPEN. A verdict says what differs, never why.

READING PRIORITY INDEX

MUST READ	Special Coverage · Ekitna · Claim Check · Evidence Card
KNOW IT	CMS rule · PITSTOP · DiaMedica · Policy watch · Calendar · Calls Ledger
SCAN	Amgen settlement · Bright spot · Registry Watch · Corrections

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01 / MARKETS & OUTLOOK TAPE, RATES, CAPITAL · AS OF THE TUESDAY 11.24 CLOSE

MARKETS & OUTLOOK

Biotech rose and tech fell on Tuesday. XBI gained 6.6% and IBB 5.2%, while QQQ fell 2.0% and SPY 0.5%. Health care was the top sector, as reported, the first session after Sanofi's Insmed deal was announced. The

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VIX eased to 26.36 and the 10-year yield to 4.91%.

BENCHMARK	11.24 CLOSE	1D	1W	1M	YTD	VS 52W HIGH
XBI (equal-weight biotech)	156.82	+6.6%	+7.9%	+4.9%	+28.6%	-7.7%
IBB (cap-weight biotech)	219.49	+5.2%	+6.1%	+5.7%	+30.1%	-1.3%
PPH (pharma)	120.01	+3.3%	-0.1%	+4.4%	+16.3%	-3.4%
XPH (equal-weight pharma)	66.87	+4.4%	+4.2%	+6.7%	+19.4%	-10.0%
SPY	718.78	-0.5%	-1.9%	-5.4%	+5.4%	-8.0%
QQQ	638.10	-2.0%	-2.9%	-9.4%	+3.9%	-16.4%
IWM	267.14	+0.5%	-0.7%	-3.1%	+8.5%	-12.5%

Price returns from Robinhood market data: 1D vs 11.23, 1W vs 11.17, 1M vs 10.23, YTD vs 12.31.2025; dividends not included. Distance from the highest intraday price since 11.25.2025. VIX 26.36 at the 11.24 close, from 26.62 on 11.23, from Robinhood index data DATA. XLV (health care) closed at 184.72, up 3.0%, from Robinhood market data DATA.

Rates & macro

Fed funds target	**3.75 to 4.00%**	Held 10.28 by a 10 to 2 vote; both dissents preferred a hike
UST 2Y / 10Y	**4.63% / 4.91%**	11.24; 10Y down 1bp from 11.23
December FOMC	**Hike priced, as reported**	About 95% to 96% odds of a quarter-point hike at the 12.08 to 12.09 meeting, the rest a half point, per CappNotes (11.24)
VIX	**26.36**	11.24 close; 26.62 on 11.23

Biotech capital, YTD

Financings counted	**747 / $87.9B**	Mind Club tally, 11.25; see 02
US IPOs	**30 / ~$8.2B**	US biotech IPOs in the Mind Club tally, 11.25
M&A value	**Not available**	No primary-based year-to-date figure found; see 06 for deals

U.S. Treasury daily par yield curve (11.24) GOV; FOMC statement (10.28) and FOMC calendar GOV; CME FedWatch odds as reported by CappNotes (11.24) PRESS; sector ranking as reported by CappNotes (11.24) PRESS; Mind Club financing tally DATA.

THE DAY'S MACRO DRIVER

AI stocks fell back on Tuesday after Monday's rally: Nvidia fell 5.9% and Anthropic closed below its $83 IPO price, per the Associated Press (11.24) PRESS. Biotech went the other way, and XBI beat QQQ by about 8.6 points in one session. Biotech cares because the same rate path weighs on both: a December hike is priced in futures, as reported, and today's 8:30 am ET PCE inflation reading, as reported, is the last major one before the 12.09 decision. A hotter print could revive talk of a half-point move. ANALYSIS

RED TEAM

A 6.6% day on one deal can reverse fast, and part of the move may be money leaving AI stocks rather than a new view on biotech. The hike odds come from a newsletter's reading of CME, not from CME directly. ANALYSIS

2026 CAPITAL SCORECARD

One financing of $5M or more counted from the window: DiaMedica's $86 million public offering, priced on Tuesday. The tally stands at 747 deals and $87.9B, from 746 and $87.8B on 11.24.

CHANNEL	US	REST OF WORLD	AS OF	READ
IPOs	30 · $8.2B	18 · $2.2B	11.25	No new pricing in the window; Alopexx amended its registration for a long-pending IPO (see 07)
Venture rounds	188 · $14.9B	176 · $16.3B	11.25	No new round counted today; the Saturday sweep may add smaller or non-US rounds
Follow-ons, PIPEs & RM	272 · $42.4B	63 · $3.8B	11.25	DiaMedica's base offering counted; any underwriter option excluded
Total tracked	**490 · $65.6B**	**257 · $22.3B**	11.25	US is close to complete; rest of world is directional
M&A (context)	No new acquisition with stated terms in the window		11.25	See 06 and 04S

Two Isomorphic Labs rounds ($7.1B) make about 44% of rest-of-world venture dollars. ANALYSIS

Mind Club financing tally, 2026 financings of $5M or more of new money, base gross upfront, deal by deal with a source for each row DATA. Dollar figures are rounded.

RED TEAM

A day before a holiday says little about the financing window. One $86 million offering is about 0.1% of the year's total, so today's count is a pulse, not a trend. ANALYSIS

WHERE THE MONEY WENT

DiaMedica's offering is counted in US cardiovascular and renal follow-on money, by its lead program in preeclampsia. Brand blue deepens with dollars.

United States 490 FINANCINGS · $65.6B

THERAPEUTIC AREA	IPOS	VENTURE ROUNDS	FOLLOW-ONS, PIPES & RM	TOTAL
Oncology	$1.7B	$3.5B	$12.8B	$18.0B
Immunology & inflammation	$1.9B	$2.8B	$11.7B	$16.4B
Neuroscience & pain	$741M	$1.3B	$5.9B	$7.9B
Rare & genetic	$1.0B	$1.4B	$4.6B	$7.0B
Obesity & metabolic	$706M	$1.2B	$1.9B	$3.8B
Cardiovascular & renal	$1.2B	$428M	$2.2B	$3.8B
Other	$448M	$1.6B	$1.1B	$3.2B
Infectious disease & vaccines	·	$515M	$1.6B	$2.1B
AI & platform	$400M	$1.1B	$300M	$1.8B
Ophthalmology	$150M	$1.1B	$322M	$1.6B
TOTAL	$8.2B	$14.9B	$42.4B	$65.6B

Rest of world 257 FINANCINGS · $22.3B

EUROPE 101 · CHINA & HK 90 · KOREA 23 · AUSTRALIA & NZ 11 · CANADA 10 · JAPAN 8 · OTHER 14

THERAPEUTIC AREA	IPOS	VENTURE ROUNDS	FOLLOW-ONS, PIPES & RM	TOTAL
AI & platform	$270M	$9.3B	$92M	$9.6B
Oncology	$602M	$3.0B	$2.1B	$5.7B
Immunology & inflammation	$351M	$849M	$224M	$1.4B
Rare & genetic	·	$772M	$574M	$1.3B
Neuroscience & pain	·	$1.0B	$168M	$1.2B
Cardiovascular & renal	$534M	$452M	$28M	$1.0B
Other	$205M	$211M	$325M	$742M
Infectious disease & vaccines	$227M	$144M	$145M	$516M
Obesity & metabolic	·	$282M	$121M	$403M
Ophthalmology	$42M	$288M	$5M	$335M
TOTAL	$2.2B	$16.3B	$3.8B	$22.3B

LESS MORE

One scale across both tables: channel columns together, totals separately.

Coverage: 747 disclosed 2026 financings of $5M or more, $87.9B in total. US means raised on a US exchange or, for private rounds, by a US-headquartered company. Rest of world covers money raised on non-US exchanges or, for private rounds, by companies headquartered outside the US: mainly mainland China and Hong Kong, Europe, South Korea, Japan, Australia and Canada. A US company raising on a non-US exchange counts as rest of world. Base gross upfront new money; excludes debt, standalone convertibles, at-the-market sales, grants, unexercised warrants and money raised before 2026. Sourced deal by deal in the Mind Club financing tally. US is close to complete; read rest of world as directional. Therapeutic area by lead program.

03 / OUTLOOK THE NEXT 30, 60 AND 90 DAYS

OUTLOOK

Our view holds. Tuesday's biotech gain came the first session after the Sanofi deal, and followed a broad Monday rebound, so it does not change yesterday's view. Today's PCE reading and the 12.09 FOMC remain the near-term tests.

HORIZON	WHAT WE EXPECT	WHAT WOULD CHANGE IT	ODDS
30 days	Vertex's 11.30 goal date, today's PCE reading and the 12.09 FOMC, where a hike is priced in futures, as reported, set the news flow	A hold or a 50 basis point move at the 12.09 FOMC	·
60 days	SABCS (12.08 to 12.11), ASH (12.12 to 12.15) and December goal dates lead the calendar	Another large acquisition, which would suggest Sanofi's deal is part of a run	·
90 days	Insmed shareholders and regulators review the Sanofi deal, with closing expected in the first half of 2027	A rival bid or a regulatory objection	·

Dates from 14 Verified Catalyst Calendar; odds only where a logged call in 15 sets them, and none is open today. ANALYSIS

Scenarios for the sector, next 90 days

CASE	WHAT IT LOOKS LIKE	ODDS
Bull	PCE and the 12.09 decision land as priced, more buyers follow Sanofi, and biotech keeps leading the broad market	25%
Base	Biotech trades on its own calendar of readouts and goal dates, holds most of its year-to-date gain, and swings with a VIX in the mid-20s	55%
Bear	A half-point hike or a hawkish set of projections at the 12.09 meeting, with the AI selloff spreading, takes back the deal-day gains	20%

Odds are our subjective judgment, not a forecast logged in 15 and not advice. ANALYSIS

What changed since yesterday

Little. XBI rose 6.6% on 11.24 while QQQ fell 2.0%, the first session after the Sanofi announcement. December hike odds stayed near certain, as reported, with a small share now on a half point. Neither moves our 30, 60 or 90 day view. ANALYSIS

RED TEAM

One $41B deal does not make a cycle: buyers may pay up for an approved, growing drug and still pass on earlier assets. One day of biotech beating tech may reflect rotation out of AI more than demand for biotech, and our scenario odds rest on judgment, not a model. ANALYSIS

04 / FIVE THINGS TO KNOW TUE 11.24 AM TO WED 11.25 AM PT

FIVE THINGS TO KNOW

An early GIST approval, a Medicare rule opening for comment, and a large sepsis trial that found no gain from moving treatment into the ambulance. Sanofi and Insmed run as Special Coverage in 04S.

01 FDA approved Cogent's Ekitna (bezuclastinib) with sunitinib for advanced GIST after imatinib MUST READ

WHAT HAPPENED

FDA approved Ekitna, from Cogent Biosciences, with sunitinib on 11.24 for adults with advanced gastrointestinal stromal tumors (GIST) previously treated with imatinib, six days before the 11.30 goal date. It is the 57th entry on FDA's 2026 novel approvals list. In the Phase 3 PEAK trial (413 patients), median progression-free survival was 16.5 months with the combination vs 9.2 months with sunitinib alone (hazard ratio 0.50). Overall survival was not mature. The label carries a

boxed warning for liver toxicity. Cogent says the drug is available now. Neither FDA nor Cogent says whether the approval is full or accelerated. VERIFIED

WHY IT MATTERS

KIT mutations drive most GIST, and resistance after imatinib is common. Ekitna adds a selective KIT inhibitor to sunitinib rather than replacing it, so its place depends on whether the progression-free gain holds up in survival and against liver risk. ANALYSIS

WHAT WE'RE WATCHING

PEAK's overall survival data, uptake, and Cogent's nonadvanced systemic mastocytosis application, with a 12.30.2026 goal date, and its advanced systemic mastocytosis application, with a 06.29.2027 goal date, per its third quarter 10-Q.

CLAIM CHECK MATCH NCT05208047 registers progression-free survival as the Part 2 primary, the endpoint reported. The record lists 482 participants (estimated) across all parts, against 413 cited by FDA.

FDA (11.24) and Novel Drug Approvals 2026 GOV; Cogent release (11.24) CO; NCT05208047 REG

02 CMS proposed its 2028 Medicare Advantage and Part D rule; comments close 01.19.2027

KNOW IT

WHAT HAPPENED

CMS's proposed rule for contract year 2028 was published in the Federal Register on 11.25. It covers marketing, drug coverage, enrollment and special needs plans, and would set up a mandatory Medicare Advantage model at the CMS Innovation Center. Comments are due 01.19.2027. VERIFIED

WHY IT MATTERS

Part D coverage terms for 2028 are open for comment. We have read the abstract only, so we do not yet say what the drug provisions change. ANALYSIS

WHAT WE'RE WATCHING

The full text's Part D provisions and comments from plans and drugmakers.

Federal Register (11.25) GOV

03 PITSTOP: antibiotics or extra fluids in the ambulance did not lower sepsis deaths KNOW IT

WHAT HAPPENED

Two JAMA papers on 11.24 report PITSTOP, a randomized 2 × 2 factorial trial run by Ontario paramedic services in adults with suspected sepsis and low blood pressure. Hospital mortality to day 90 was 18.0% with intramuscular ceftriaxone vs 18.4% with placebo (risk ratio 0.97, 95% CI 0.81 to 1.17; 2,091 randomized), and 18.0% with liberal fluids vs 18.3% with usual care (risk ratio 0.98, 95% CI 0.80 to 1.20; 1,686 randomized). VERIFIED

WHY IT MATTERS

It tests the idea that every hour counts for antibiotics in sepsis and found no survival gain from moving the first dose into the ambulance. The intervals still allow a modest benefit or harm. ANALYSIS

WHAT WE'RE WATCHING

Whether paramedic sepsis protocols change, and subgroup data in septic shock.

CLAIM CHECK PARTIAL NCT03068741 registers the same primary outcome. The record lists Phase 4 and 2,061 enrolled, while the antibiotic paper reports 2,091 randomized; the record does not explain the gap.

JAMA, antibiotics (11.24) and JAMA, fluids (11.24) PEER; NCT03068741 REG

04 DiaMedica priced an $86 million offering, with a top five pharma company among the buyers, per the company KNOW IT

WHAT HAPPENED

DiaMedica priced 10,750,000 shares at $8.00 on 11.24, about $86.0 million gross, and said new healthcare investors led the offering and a top five global pharma company invested; it did not name the company. The money funds DM199, a recombinant form of the enzyme tissue kallikrein-1, in preeclampsia and fetal growth restriction. The same morning it reported interim Phase 2 data in fetal growth restriction: of 10 women with known delivery dates, nine stayed pregnant past the published historical median, in a single-arm study of 12 with no serious adverse events, by the company's account. VERIFIED

WHY IT MATTERS

A large pharma buying into an offering is a signal of interest, not a deal. The data are small, uncontrolled and set against historical medians (see 08). ANALYSIS

CLAIM CHECK PARTIAL The ClinicalTrials.gov entry, NCT06875141, is withdrawn and points to a Pan African registry record we did not open; it names safety as the primary, not pregnancy prolongation.

DiaMedica 8-K Exhibit 99.1 (11.24) and data release (11.24) CO

05 Amgen settled its Opdivo biosimilar patent case; a U.S. launch is set for 10.01.2028, subject to FDA approval SCAN

WHAT HAPPENED

Amgen settled U.S. patent litigation with Bristol Myers Squibb and Ono over ABP 206, its proposed biosimilar to Opdivo (nivolumab). The settlement allows a U.S. launch on 10.01.2028, subject to FDA approval; terms are confidential. VERIFIED Separately, Pharming said on 11.25 it paused Ruconest fill-finish manufacturing and expects U.S. supply constraints. CLAIM

Amgen 8-K Exhibit 99.1; Pharming 6-K (11.25) CO

BRIGHT SPOTRibocure's Phase 2b of vortosiran, an siRNA tested in atrial fibrillation, moved to recruiting on ClinicalTrials.gov this week, with an actual start of 10.15.2026 and 150 participants planned. One more gene-silencing drug is now in trials in a common heart disease. VERIFIED NCT07870889 REG

04S / SPECIAL COVERAGE: SANOFI, INSMED AND THE I&I DEAL MARKET

SPECIAL COVERAGE · EDITION 056 ONLY

THE BIGGEST I&I DEAL IN OUR COUNT, AND WHAT BUYERS HAVE PAID FOR SINCE 2019

Sanofi's $41.0 billion cash offer for Insmed is the largest acquisition in immunology and inflammation in our count of 26 such deals since 2019, ahead of Amgen and Horizon at $27.8 billion. Here is our ledger, how I&I compares with oncology and everything else, what buyers have paid for, where China fits, and the dates that matter in 2027.

Sources: SEC filings and the releases filed with them, counted by Mind Club; FDA records; company annual reports. Our counts follow the rules printed in each section. Mind Club takes no position on any company or security and names no company as a likely target.

THE SHORT VERSION

I&I buyers have paid most for approved drugs, and 2026 is already the biggest year in our count. Nine of our 26 I&I deals bought an approved drug, and those nine carry $106.3 billion of the $178.2 billion total. VERIFIED 2026 has four deals worth $56.3 billion, the most of any year since 2019, and Insmed alone is $41.0 billion of it. VERIFIED Among listed targets since 2023, the typical I&I deal is no bigger than the typical oncology or other deal: medians of $4.05 billion, $4.10 billion and $4.30 billion. VERIFIED What sets I&I apart is a few very large bets on approved inflammation drugs, and Sanofi's is the largest. ANALYSIS Behind the deals, China-based companies sponsor 37.9% of new I&I drug trials on ClinicalTrials.gov, up from 7.5% in 2019, and one of them has an oral DPP1 drug in Phase 3 against Brinsupri's disease. VERIFIED

1 · The deal, and why we count it as I&I

Sanofi agreed to buy Insmed for $175 per share in cash, "a total equity value of approximately $41.0 billion (€37.6 billion)," about a 46% premium to Insmed's unaffected close of 11.18.2026, the day before media reports of talks. VERIFIED The companies expect to close in the first half of 2027, subject to a vote of more than two-thirds of all votes entitled to be cast, U.S. and certain non-U.S. regulatory approvals and other conditions. VERIFIED The outside date is 08.23.2027, extendable to 11.23.2027 and then 02.23.2028 only if regulatory conditions alone remain open. VERIFIED

Sanofi buys two approved drugs and a pipeline. Brinsupri (brensocatib), an oral DPP1 inhibitor approved by FDA on 08.12.2025 for non-cystic fibrosis bronchiectasis, brought in $1.09 billion following its U.S. launch in August 2025 through 09.30.2026, about 13.5 months; the release does not split the figure by country. VERIFIED Arikayce is an inhaled antibacterial for MAC lung disease. TPIP, an inhaled treprostinil prodrug, is in Phase 3 in pulmonary hypertension, with a Phase 3 in idiopathic pulmonary fibrosis planned to start in the first half of 2027; it is not approved anywhere. VERIFIED

The merger agreement sets a $1.125 billion termination fee payable by Insmed in specified cases (Section 7.3(b)). It sets no fee payable by Sanofi; Insmed can instead seek specific performance, that is, sue to force the deal through (Section 8.6(b)), and Sanofi's obligation to close is not conditioned on financing (Section 3.6(d)). VERIFIED

HOW WE CLASSIFY IT

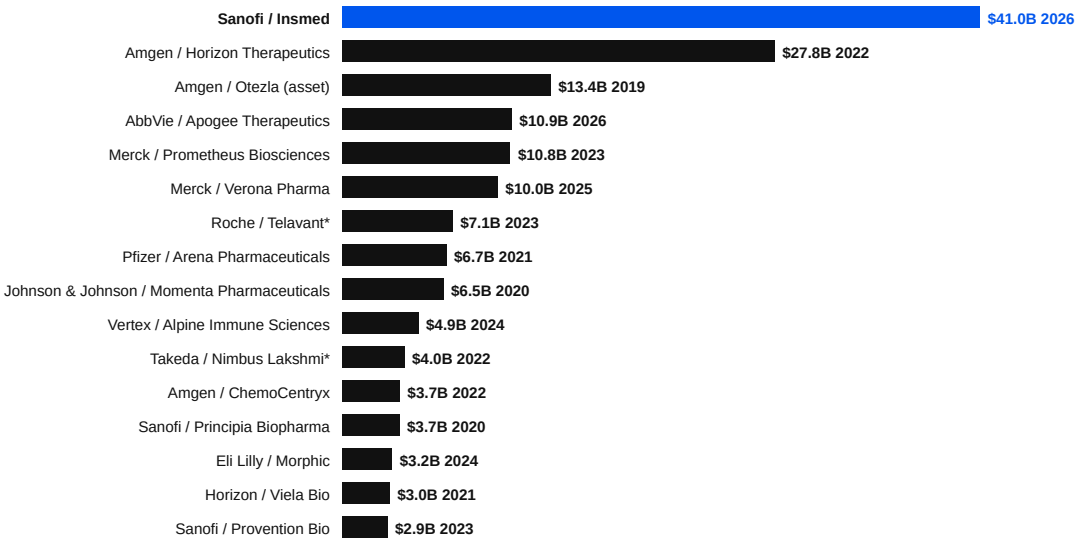
The release calls Brinsupri "a first-in-class DPP1 inhibitor targeting neutrophilic inflammation." VERIFIED Bronchiectasis is an inflammatory lung disease driven by neutrophils, so we count the deal as I&I, in respiratory inflammation, at the edge of classic immunology. We count Merck's purchase of Verona (Ohtuvayre, for COPD) the same way. Arikayce, an antibiotic, and TPIP, a pulmonary hypertension drug, are not I&I; we classify every deal by its lead asset, and Brinsupri is the lead here. ANALYSIS

2 · The ledger: every I&I acquisition of $1 billion or more since 2019

Our definition. I&I: diseases driven by the immune system or by inflammation, where the lead asset acts on that process. It includes dermatology (atopic dermatitis, psoriasis, vitiligo), respiratory inflammation (COPD, bronchiectasis), GI inflammation (ulcerative colitis, Crohn's, celiac), rheumatology, allergy, and autoimmune disease of the blood, kidney, eye, nerve and endocrine systems when the drug acts on the immune system. **Counted:** acquisitions of a company, or of a lead asset outright, announced 01.01.2019 to 11.24.2026, with a stated value of $1 billion or more at announcement, cash or stock. **Value:** as the acquirer or target states it in its SEC filing (equity value where given; for private companies, the upfront); contingent value rights and milestones are left out. **Not counted:** licenses, options, minority stakes, reverse mergers. **Source rule:** each row opened at an SEC filing tonight. Listed targets found through every tender and merger filing by drug companies on EDGAR; private deals through the buyer's filings.

The largest I&I acquisitions since 2019, by stated value

VERIFIED



$B as each acquirer or target states it at announcement. * private company; values for private deals are the upfront. Top 16 of 26. Our count, SEC EDGAR filings.

Sanofi and Insmed is about 1.5 times the next largest, Amgen and Horizon in 2022.

#	BUYER	TARGET	VALUE	ANNOUNCED	CLOSED	LEAD ASSET: TARGET; DISEASE	STAGE
1	**Sanofi**	**Insmed**	**$41.0B**	**11.24.2026**	**pending**	**Brinsupri (brensocatib): DPP1 inhibitor; non-cystic fibrosis bronchiectasis**	**Approved**
2	Amgen	Horizon Therapeutics	$27.8B	12.12.2022	10.06.2023	Tepezza: IGF-1R; thyroid eye disease	Approved
3	Amgen	Otezla (asset, from Celgene/BMS)	$13.4B	08.26.2019	closed (date not counted)	Otezla (apremilast): PDE4 inhibitor; psoriasis, psoriatic arthritis	Approved
4	AbbVie	Apogee Therapeutics	$10.9B	06.22.2026	09.03.2026	zumilokibart: IL-13; atopic dermatitis	Phase 2
5	Merck	Prometheus Biosciences	$10.8B	04.17.2023	06.16.2023	tulisokibart: TL1A; ulcerative colitis, Crohn's disease	Phase 2
6	Merck	Verona Pharma	$10.0B	07.08.2025	10.07.2025	Ohtuvayre: PDE3/PDE4 inhibitor; COPD	Approved
7	Roche	Telavant (private, Roivant)	$7.1B	11.13.2023	closed (date not counted)	RVT-3101 (afimkibart): TL1A; ulcerative colitis, Crohn's disease	Phase 2
8	Pfizer	Arena Pharmaceuticals	$6.7B	12.13.2021	03.11.2022	etrasimod: S1P receptor modulator; ulcerative colitis	Phase 3
9	Johnson & Johnson	Momenta Pharmaceuticals	$6.5B	08.19.2020	10.01.2020	nipocalimab: FcRn; autoantibody diseases	Phase 2
10	Vertex	Alpine Immune Sciences	$4.9B	04.10.2024	05.20.2024	povetacicept: BAFF/APRIL; IgA nephropathy	Phase 2
11	Takeda	Nimbus Lakshmi (private)	$4.0B	12.13.2022	closed (date not counted)	TAK-279 (zasocitinib): TYK2 inhibitor; psoriasis	Phase 2
12	Amgen	ChemoCentryx	$3.7B	08.04.2022	10.20.2022	Tavneos: C5a receptor; ANCA-associated vasculitis	Approved
13	Sanofi	Principia Biopharma	$3.68B	08.17.2020	09.28.2020	rilzabrutinib: BTK inhibitor; immune thrombocytopenia	Phase 3

#	BUYER	TARGET	VALUE	ANNOUNCED	CLOSED	LEAD ASSET: TARGET; DISEASE	STAGE
14	Eli Lilly	Morphic	$3.2B	07.08.2024	08.16.2024	MORF-057: alpha4beta7 integrin; ulcerative colitis	Phase 2
15	Horizon	Viela Bio	$3.05B	02.01.2021	03.15.2021	Uplizna: CD19; NMOSD	Approved
16	Sanofi	Provention Bio	$2.9B	03.13.2023	04.27.2023	Tzield: CD3; type 1 diabetes (delay)	Approved
17	Nestle	Aimmune Therapeutics	$2.6B	08.31.2020	10.19.2020	Palforzia: peanut oral immunotherapy; peanut allergy	Approved
18	Eli Lilly	DICE Therapeutics	$2.4B	06.20.2023	08.09.2023	DC-806: IL-17 (oral); psoriasis	Phase 2
19	GSK	RAPT Therapeutics	$2.2B	01.20.2026	03.03.2026	ozureprubart: IgE; food allergy	Phase 2
20	argenx	Forte Biosciences	$2.2B	07.27.2026	08.27.2026	FB102: CD122 (IL-2/IL-15 receptor beta); vitiligo, celiac disease	Phase 1
21	UCB	Ra Pharmaceuticals	$2.1B	10.10.2019	04.02.2020	zilucoplan: complement C5; generalized myasthenia gravis	Phase 3
22	Sanofi	Kadmon	$1.9B	09.08.2021	11.09.2021	Rezurock: ROCK2 inhibitor; chronic graft-versus-host disease	Approved
23	Merck	Pandion Therapeutics	$1.85B	02.25.2021	04.01.2021	PT101: IL-2 mutein; ulcerative colitis, lupus	Phase 1
24	Biogen	HI-Bio (private)	$1.15B	08.01.2024	closed (date not counted)	felzartamab: CD38; antibody-mediated rejection, kidney disease	Phase 2
25	Eli Lilly	Dermira	$1.1B	01.10.2020	02.20.2020	lebrikizumab: IL-13; atopic dermatitis	Phase 3
26	Sanofi	Kymab (private)	$1.1B	01.11.2021	closed (date not counted)	KY1005 (amlitelimab): OX40L; atopic dermatitis	Phase 2

26 deals, $178.2 billion in all. Values and dates VERIFIED at the SEC filing named in our figure list, available on request; stage is our classification ANALYSIS . Announced: filing date of the document stating the terms. Closed: the target's 8-K reporting completion. Five rows have no counted close date: four private deals and the Otezla asset purchase. Value bases differ where the filing gives only one: ChemoCentryx (enterprise value), Ra Pharmaceuticals (net of cash), Verona (transaction value).

AT THE EDGE: DEALS WE DID NOT COUNT AS I&I

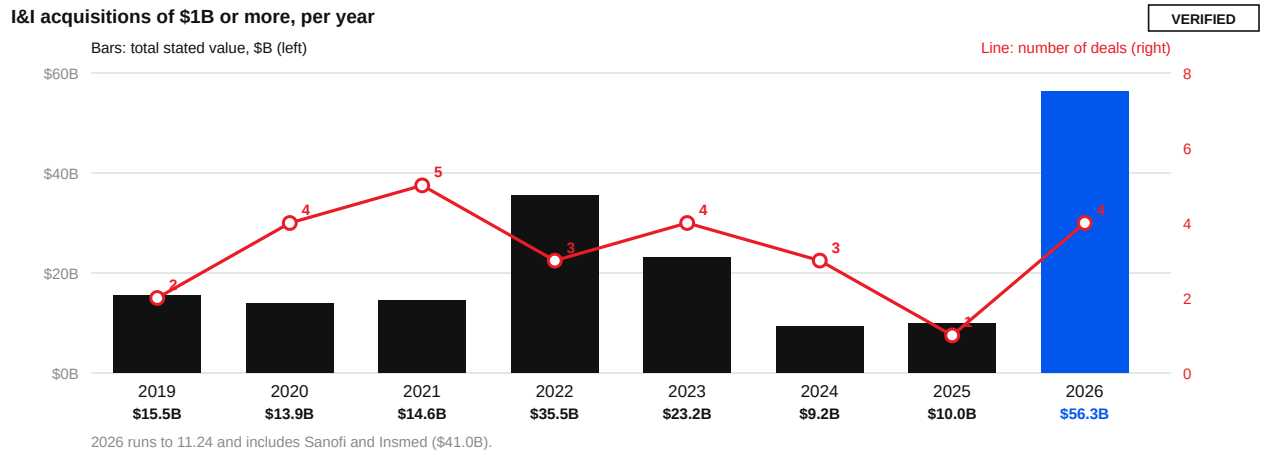
BUYER	TARGET	VALUE	ANNOUNCED	WHY NOT I&I UNDER OUR RULE
AstraZeneca	Alexion	$39.0B	12.12.2020	Soliris, Ultomiris: complement C5; lead use PNH, a blood disorder
Novartis	Chinook Therapeutics	$3.2B	06.12.2023	atrasentan, an endothelin blocker, for IgA nephropathy
Gilead	CymaBay	$4.3B	02.12.2024	seladelpar, a PPAR delta agonist, for primary biliary cholangitis
Sanofi	Blueprint Medicines	$9.1B	06.02.2025	Ayvakit, a KIT inhibitor, for systemic mastocytosis; Sanofi files it under immunology
Novartis	Tourmaline Bio	$1.4B	09.09.2025	pacibekitug, an IL-6 antibody, for cardiovascular inflammation
Eli Lilly	Ventyx Biosciences	$1.2B	01.07.2026	NLRP3 inhibitors for pericarditis, cardiovascular risk and Parkinson's disease
Biogen	Apellis	$5.6B	03.31.2026	pegcetacoplan, a C3 inhibitor; lead use geographic atrophy, an eye disease; Biogen calls it immunology

Counted in "all other areas" in section 3. Counting all seven as I&I would add $63.8 billion; AstraZeneca and Alexion ($39.0 billion) would then rank second, behind Insmed. The line is ours, not an industry standard, and other trackers may draw it differently, which would change the totals. ANALYSIS

FOUND BUT NOT COUNTED TONIGHT

BUYER	TARGET	YEAR	LEAD ASSET	WHY LEFT OUT
AbbVie	Capstan Therapeutics (private)	2025	in vivo CD19 CAR-T, autoimmune	reported up to $2.1B; upfront not confirmed at a primary source tonight
Bristol Myers Squibb	Orbital Therapeutics (private)	2025	in vivo CAR-T, autoimmune	reported $1.5B; not confirmed at a primary source tonight
Johnson & Johnson	Yellow Jersey (private)	2024	NM26, IL-4R and IL-31 bispecific, atopic dermatitis	reported $1.25B; J&J release confirms completion, not the price
Eli Lilly	Orna Therapeutics (private)	2026	in vivo CD19 CAR-T, B-cell autoimmune	reported up to $2.4B; Lilly filings confirm the deal, not an upfront
Gilead and Lakefront	Ouro Medicines (private NewCo)	2026	CM336, BCMA x CD3 bispecific licensed from Keymed (China), autoimmune	completed 06.05.2026 per Keymed's release; price not disclosed
Eli Lilly	Merida Biosciences (private)	2026	autoantibody removal, Graves' disease	Lilly states up to $2.875B including milestones; upfront not disclosed

Headline values from press reports CLAIM . Each would be counted once its upfront is confirmed in a filing.



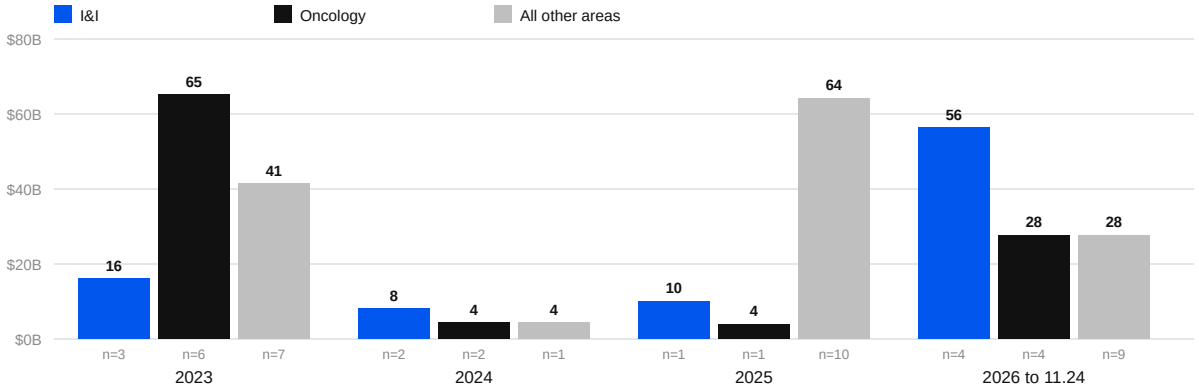
Our count of 26 deals, 2019 to 11.24.2026. Values as stated at announcement; private deals at upfront. SEC EDGAR filings.

2022 and 2026 are the two big years, each made by one deal: Horizon and Insmed.

3 · I&I against oncology and everything else

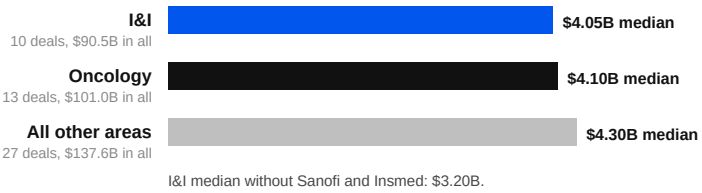
To compare like with like, this section counts only **listed** targets, where the filings make the count complete: every drug company on EDGAR that filed a tender or merger statement from 01.01.2023 to 11.24.2026, with a stated value of $1 billion or more, contingent payments left out, sorted by the same lead-asset rule. Private deals drop out here, so the I&I figures are smaller than the ledger's. VERIFIED

Total stated value of $1B+ acquisitions of listed biopharma companies, by area VERIFIED



$B. Listed targets with an SEC tender or merger filing, 01.2023 to 11.24.2026; same rules for every area. Our count, SEC EDGAR.

Median deal size by area, listed targets, 01.2023 to 11.24.2026 VERIFIED



I&I median without Sanofi and Insmed: $3.20B.

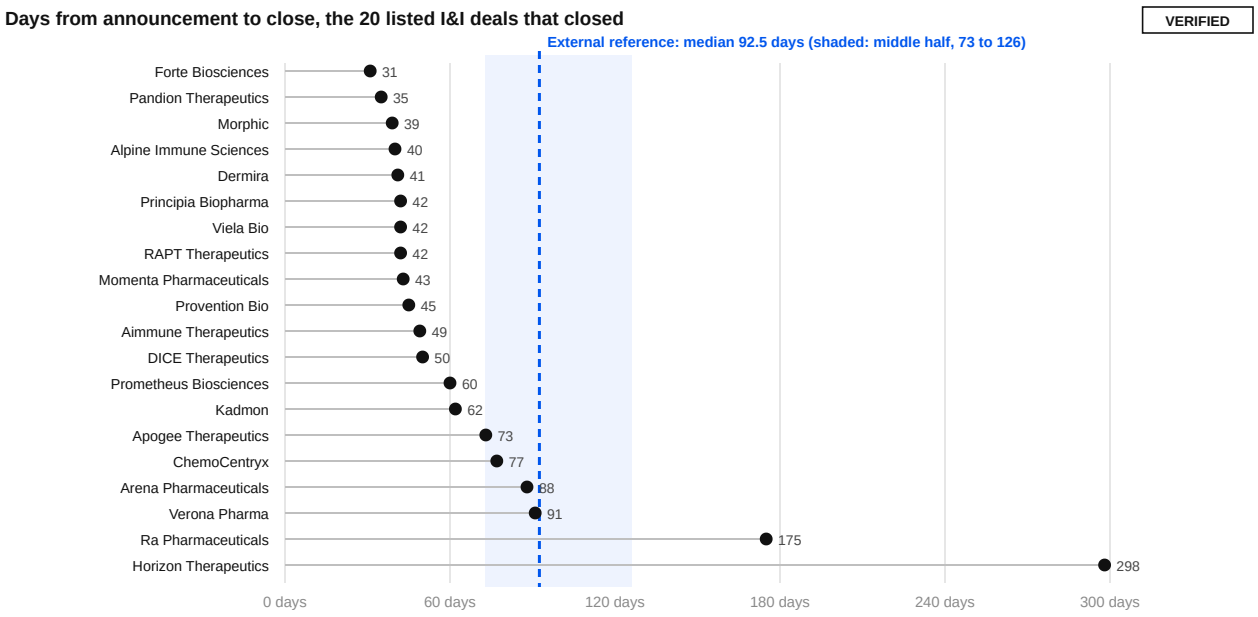
$B, stated value at announcement, contingent payments excluded. Our count, SEC EDGAR.

LISTED TARGETS, 01.2023 TO 11.24.2026	I&I	ONCOLOGY	ALL OTHER AREAS
Deals of $1B or more	10	13	27
Total stated value	$90.5B	$101.0B	$137.6B
Median deal	$4.05B	$4.10B	$4.30B
Largest deal	Insmed, $41.0B	Seagen, $43.0B	Intra-Cellular, $14.6B
2026 to date, deals and value	4, $56.3B	4, $27.6B	9, $27.8B

Our count VERIFIED . “All other areas” covers neuroscience, cardiometabolic and obesity, rare disease, eye, vaccines and infectious disease, liver and kidney, and the edge cases in section 2. Seagen’s value is the enterprise value Pfizer stated. Left out because the filing gives no value without contingent payments, or because it was not confirmed tonight: list available on request.

In 2026, I&I leads the three areas by value, on four deals, as it did in 2024 on smaller ones. VERIFIED One deal does most of that: without Insmed, 2026 I&I would be $15.3 billion. The median tells the steadier story: buyers pay about the same for a typical I&I, cancer or other target, around $4 billion. ANALYSIS

How fast these deals close matters for the calls below. The 20 listed I&I deals in our ledger that closed took a median of 47 days from terms to completion, faster than the external reference, which leaves out tender offers, the form most of ours took. VERIFIED The two slowest both needed a shareholder vote: Ra Pharmaceuticals at 175 days and Horizon at 298 days. VERIFIED

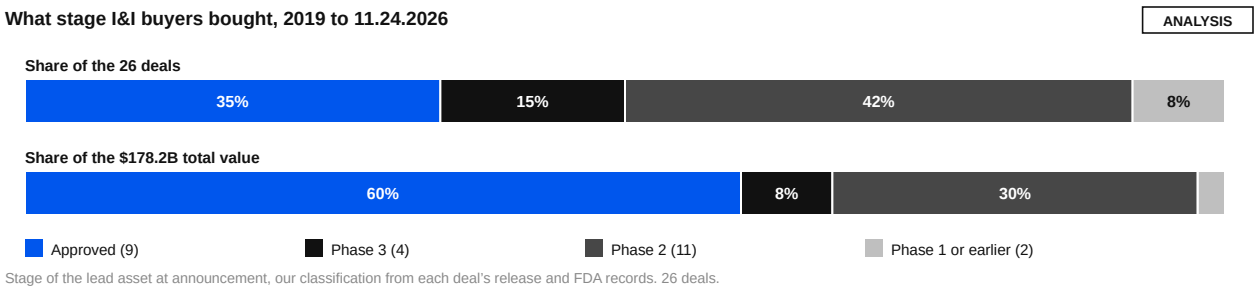


Our median: 47 days. Dates from SEC 8-K filings (terms, then Item 2.01). Reference: SEC sample, 74 biopharma mergers, 2021 to 2023, not Mind Club's record.

External reference (SEC EDGAR sample, not Mind Club's record): in 74 biotech and pharma mergers whose merger proxy was filed 2021 to 2023, the median time from merger agreement to completion was 92.5 days. That sample leaves out tender offers.

4 · Pattern recognition: what I&I buyers pay for

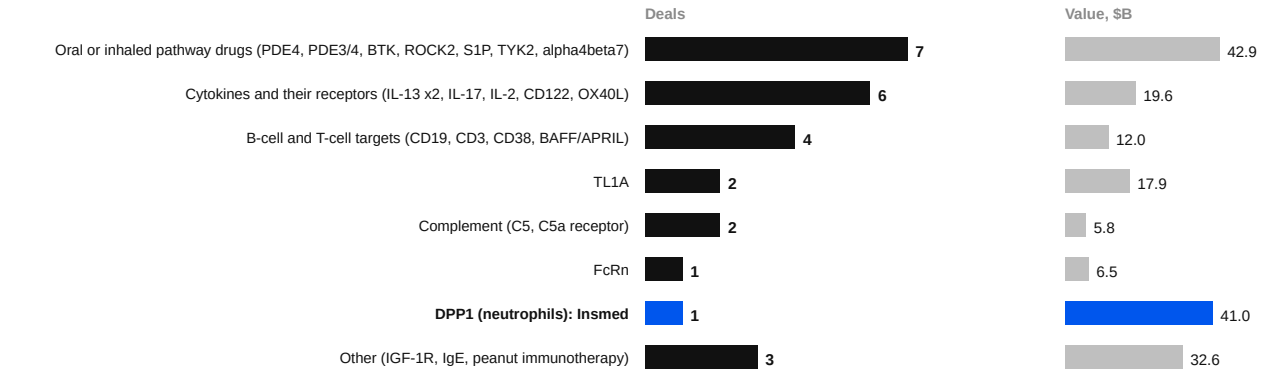
Approved drugs take the money; Phase 2 takes the count. Eleven of 26 deals bought a Phase 2 asset, the most of any stage, but the nine approved-drug deals hold 60% of the value. ANALYSIS They include three of the four largest: Insmed, Horizon and Otezla; the fourth, Apogee, was a Phase 2 bet. VERIFIED



Stage of the lead asset at announcement, our classification from each deal's release and FDA records. 26 deals.

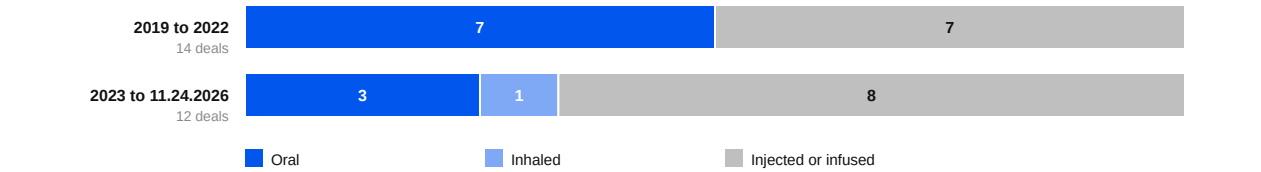
Mechanisms cluster, and the big brands are missing. Oral or inhaled drugs that act inside immune cells (PDE4, BTK, TYK2, S1P and others) are the largest group at seven deals; cytokine drugs are next at six. Buyers paid for TL1A twice in 2023, $10.8 billion and $7.1 billion, before any TL1A drug had Phase 3 data. ANALYSIS No deal in our ledger had an IL-23 or TSLP drug as its lead asset, though Apogee carries a TSLP antibody in early trials. VERIFIED DPP1, Insmed's mechanism, is a first in our ledger. ANALYSIS Pills are reaching ground held by injections: FDA approved J&J's oral icotrokinra (Icotyde) on 03.17.2026. VERIFIED It is an oral peptide aimed at the IL-23 receptor. CLAIM

Mechanisms bought: the lead asset's target in each I&I deal ANALYSIS



26 deals, 2019 to 11.24.2026. None of the 26 had an IL-23 or TSLP drug as its lead asset. Our classification from each release.

Pills, puffs or shots: how the lead asset is given ANALYSIS

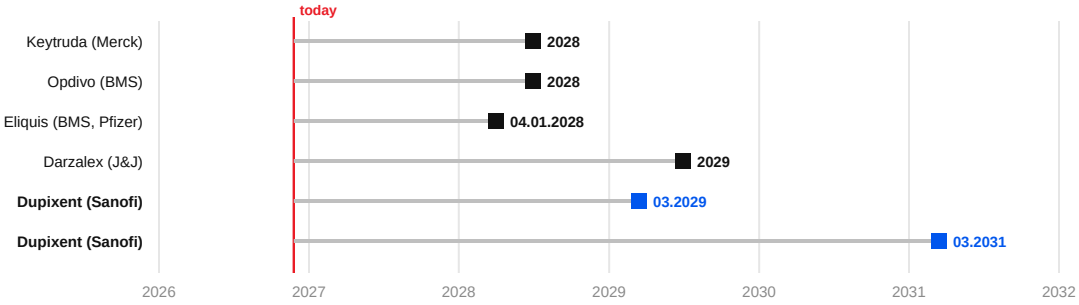


Number of I&I deals by route of the lead asset at announcement. Our classification from each release.

From 2023 the mix tilts toward injected antibodies; Insmed is the first oral approved drug bought for $1 billion or more since Amgen and ChemoCentryx in 2022.

The cliff behind it. Sanofi says Dupixent's U.S. regulatory exclusivity runs to 03.2029 and its compound patent, with extension, to 03.2031. COMPANY STATEMENT Dupixent made €15,714 million of sales in 2025. VERIFIED Merck, BMS, Pfizer and J&J each give U.S. exclusivity dates for their largest drugs between 2028 and 2029. COMPANY STATEMENT That is the backdrop to our storylines "Patent cliff buyers" and "Sanofi beyond Dupixent". ANALYSIS

The cliff behind the buying: U.S. exclusivity dates the companies give COMPANY STATEMENT



Each date as the company states it in its latest annual report (10-K or 20-F, filed 2026). Year-only dates plotted at midyear. Later patents may extend some.

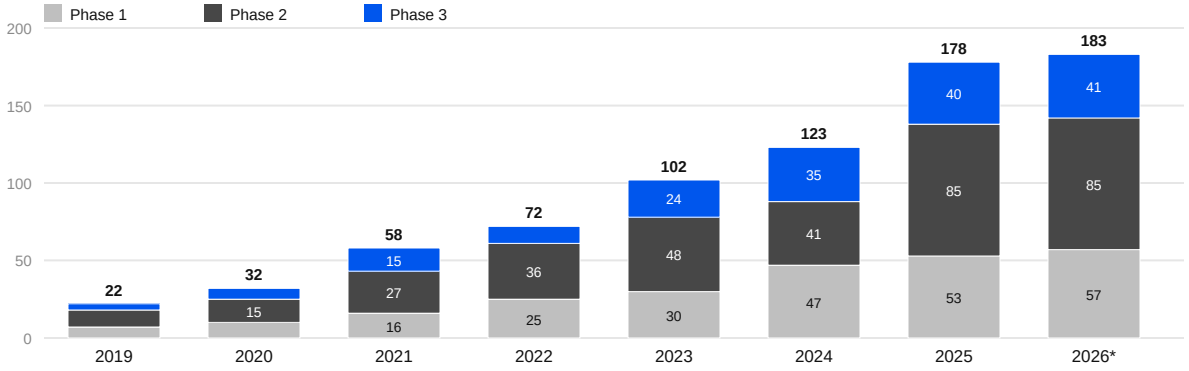
Read together, the pattern may suggest that the buyers with the nearest cliffs prefer drugs that already sell, while those with more time keep buying Phase 2 mechanisms. Our ledger is too small to show that by company, and we have not tested it; it is a reading, not a finding. ANALYSIS

5 · China: the multi-target wave

The R&D wave. We counted every industry-sponsored drug trial in our I&I diseases on ClinicalTrials.gov that started from 2019 to 2026, Phases 1 to 3: 2,889 trials. Companies based in mainland China or Hong Kong sponsor 770 of them. Their share of new trials rose from 7.5% of those starting in 2019 to 37.9% of those starting or set to start in 2026, and

from 3.6% to 31.5% of Phase 3 trials. VERIFIED Sponsors outside China with sites in the U.S. or Europe started a roughly steady 161 to 241 trials a year over the same period. VERIFIED

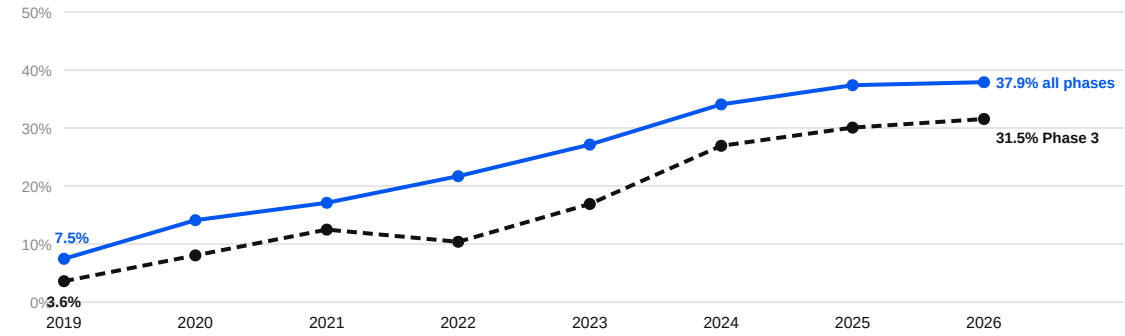
I&I drug trials sponsored by China-based companies, by start year and phase VERIFIED



* 2026 counts trials with a start date in 2026, including 88 not yet recruiting.

Industry-sponsored interventional drug trials on ClinicalTrials.gov, our count, query of 11.24.2026. Highest phase counted. 770 trials.

China-based sponsors' share of industry I&I drug trials VERIFIED

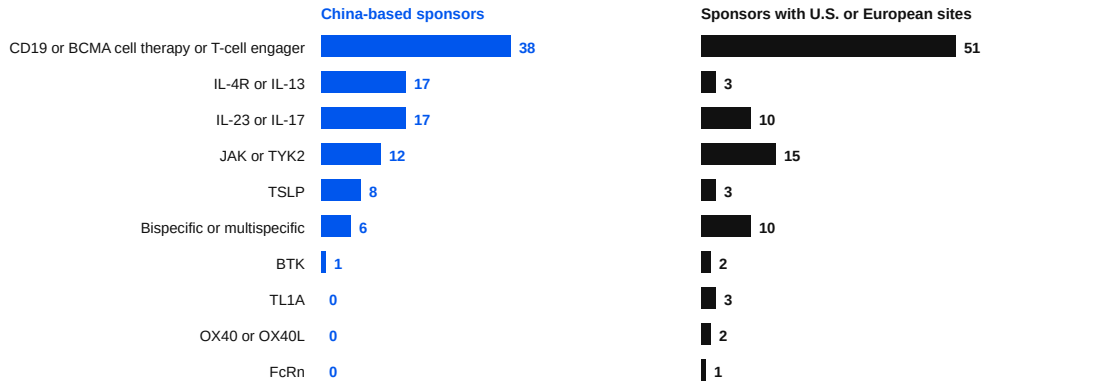


Share of industry-sponsored I&I drug trials by start year; solid: all phases, dashed: Phase 3. Our count, ClinicalTrials.gov, 2,889 trials, query of 11.24.2026.

Counted by the sponsor's base, not by where patients are enrolled. Many Chinese trials register only with China's own registry, so this is likely a floor for China.

Registry records rarely name a target: 678 of the 770 China-sponsored trials list only a code name. Among those that do, the most common are CD19 or BCMA cell therapies and T-cell engagers in autoimmune disease (38 trials, against 51 for sponsors with U.S. or European sites), then IL-4R or IL-13 and IL-23 or IL-17 (17 each). VERIFIED Those are floors; the true mix is hidden behind code names. ANALYSIS

Targets named in the registry, I&I drug trials started 2019 to 2026 VERIFIED



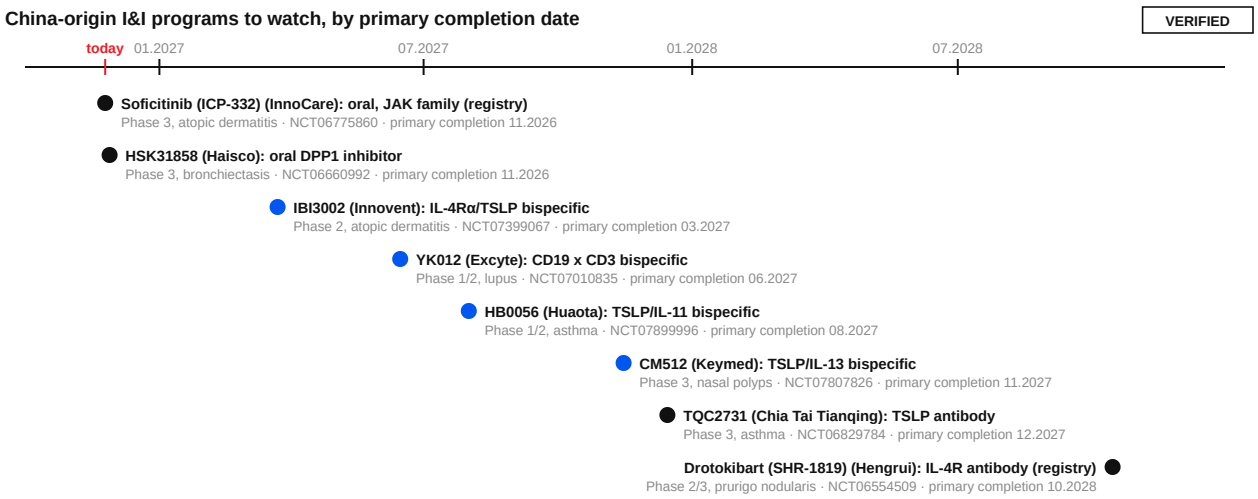
Most registry entries name a code, not a target: 678 of 770 China-sponsored trials and 1599 of 1690 others are untagged.

Counts of trials whose registry text names the target. Explicit mentions only, so these are floors, not totals. Our count, ClinicalTrials.gov, 11.24.2026.

Programs that could disrupt. Eight China-origin programs in Phase 1/2 to Phase 3 stand out because they aim at the same patients as today's biggest I&I drugs or at Brinsupri itself:

PROGRAM (SPONSOR)	TARGET, AS THE RECORD STATES IT	PHASE, INDICATION	REGISTRY ID	PRIMARY COMPLETION
HSK31858 (Haisco)	Oral DPP1 inhibitor, the same mechanism as Brinsupri	Phase 3, bronchiectasis (669 patients)	NCT06660992	11.28.2026
Soficitinib, ICP-332 (InnoCare)	Oral tablet; registry names JAK	Phase 3, atopic dermatitis	NCT06775860	11.25.2026
IBI3002 (Innovent)	IL-4Rα/TSLP bispecific	Phase 2, atopic dermatitis	NCT07399067	03.23.2027
YK012 (Excyte)	CD19 x CD3 bispecific T-cell engager	Phase 1/2, lupus	NCT07010835	06.2027
HB0056 (Huaota)	TSLP/IL-11 bispecific	Phase 1/2, asthma	NCT07899996	08.01.2027
CM512 (Keymed)	TSLP/IL-13 bispecific	Phase 3, nasal polyps; Phase 2 in asthma, atopic dermatitis, COPD and urticaria	NCT07807826	11.2027
TQC2731 (Chia Tai Tianqing)	TSLP antibody	Phase 3, asthma	NCT06829784	12.2027
Drotokibart, SHR-1819 (Hengrui)	IL-4R antibody	Phase 2/3, prurigo nodularis	NCT06554509	10.2028

Registry records on ClinicalTrials.gov, read 11.24.2026 VERIFIED . IBI3002 and CM512 targets from the sponsors' releases (Innovent, 05.2026; Keymed's first-half 2026 results); Keymed says CM512 met all Phase 2 endpoints in nasal polyps CLAIM . Primary completion dates are sponsor estimates and often move.



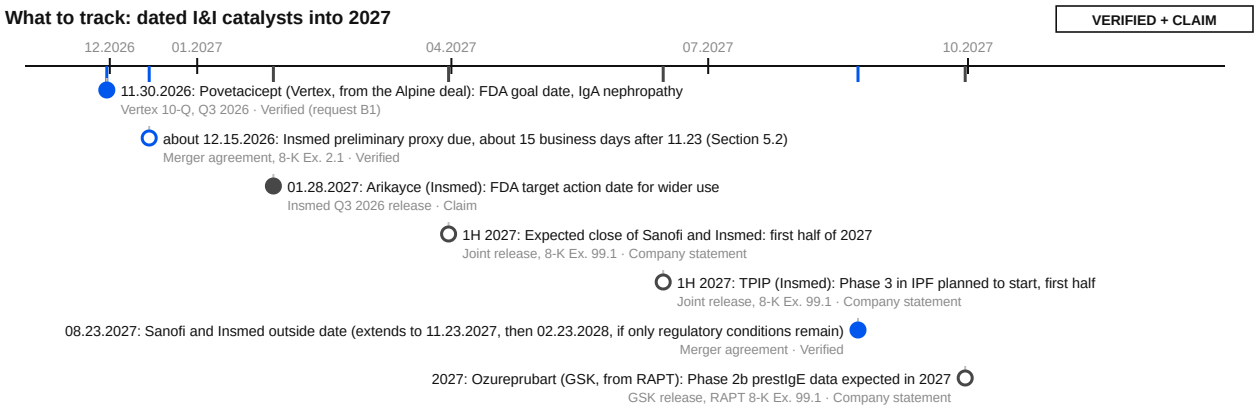
Registry dates are sponsor estimates and often move. Blue: bispecific. Targets from the registry record or the sponsor's release, as labeled in our figure list.

What it could mean, hedged. HSK31858 is the most direct: an oral DPP1 drug in Phase 3 in the same disease as Brinsupri, with a primary completion date three days from now. If it works, Sanofi may face a second DPP1 drug, at least in China. ANALYSIS The bispecifics aim at the Dupixent and Tezspire pathways at once (IL-4R or IL-13 with TSLP); if one proves better than either alone, the next fight in type 2 inflammation may be over combinations rather than single targets. Sanofi has a Phase 3 program of its own in this space, lunsekimig in COPD, with primary completion in 11.2029 (registry, VERIFIED); the record does not name its targets. ANALYSIS Keymed's antibody Kangyueda, already sold in China, brought in RMB393 million in the first half of 2026, up 132%. VERIFIED That is a home-market proof, not a Western one. ANALYSIS

How Western buyers have reached these molecules. None of the 26 acquisitions in our ledger has a bispecific or multi-target lead asset. VERIFIED The path so far has been licenses and new companies built on a license. One of those has now been bought: Gilead and Lakefront acquired Ouro Medicines, Keymed's partner for the BCMA x CD3 bispecific CM336 in autoimmune disease, completed 06.05.2026; Keymed received $257 million up front, per its first-half 2026 results release. VERIFIED The purchase price was not disclosed, so it is not in our ledger. Policy is a counterweight: comments on the U.S. outbound investment rule covered in Edition 053 close 12.07.2026. ANALYSIS

Our count of China-origin I&I licensing deals with upfronts of $50 million or more is not included: most upfronts are stated in Hong Kong exchange filings we could not open tonight.

6 · What to track in 2027



Filled dot: an exact date. Open dot: a window, plotted at its middle. Labels per item. Arikayce date not yet opened at the source tonight (Claim).

DATE	WHAT	SOURCE
11.30.2026	FDA goal date for povetacicept (Vertex, bought with Alpine) in IgA nephropathy; our call B1 prints today	Vertex 10-Q VERIFIED
about 12.15.2026	Insmed's preliminary proxy due, 15 business days from 11.23 (Section 5.2); our call B2 prints today	Merger agreement VERIFIED
11.28.2026	Primary completion of Haisco's Phase 3 of HSK31858, an oral DPP1 drug, in bronchiectasis (estimate)	NCT06660992 VERIFIED
01.28.2027	FDA target action date for wider use of Arikayce	Insmed Q3 release CLAIM
1H 2027	Expected close of Sanofi and Insmed; Phase 3 of TPIP in IPF planned to start	Joint release COMPANY STATEMENT
08.23.2027	Outside date of the Insmed merger agreement, extendable twice for regulatory conditions only	Merger agreement VERIFIED
09.30.2027	Latest primary completion among Sanofi's six Phase 3 trials of amlitelimab (OX40L) in atopic dermatitis (estimate)	NCT06241118 VERIFIED
2027	Phase 2b prestIgE data for ozureprubart (GSK, bought with RAPT) in food allergy	GSK release COMPANY STATEMENT
05.2028	First primary completion among Sanofi's four Phase 3 trials of duvakitug in UC and Crohn's (estimate)	NCT07184996 VERIFIED
03.2029	Dupixent U.S. regulatory exclusivity ends, as Sanofi states it	Sanofi 20-F COMPANY STATEMENT

A NEW CALL

CALL	ODDS	BASE RATE	RESOLVES ON
S1. A biopharma company announces a definitive agreement to acquire an I&I company or I&I lead asset, under the definition in section 2, with a stated value of $1.0 billion or more, between 11.25.2026 and 03.31.2027 (ET).	65%	68%: our ledger's pace of 26 deals in 2,884 days, about 1.14 expected in a 126-day window (Poisson; our count)	The buyer's press release (fallback: the SEC 8-K with the terms)

S1 test: yes on a signed definitive agreement; licenses, options and reverse mergers do not count; a value stated only with contingent payments counts only if the upfront alone is $1.0 billion or more. Next dated fact: the J.P. Morgan Healthcare Conference, 01.11 to 01.14.2027. S1 does not duplicate B3 ($5.0 billion or more, any area, to 01.15.2027); a deal can resolve both. Nothing here is a view on any company or security. FORECAST

7 · Where this could be wrong

RED TEAM: "INSMED IS NOT REALLY AN I&I DEAL"

Bronchiectasis is treated by lung doctors, and the release sells Sanofi a position in respiratory medicine. Counting it as I&I could flatter a record-year story. **What would settle it:** how the companies and FDA describe the label as it widens; on our rule, Brinsupri's mechanism (neutrophilic inflammation) keeps it in. If you drop it, 2026 I&I falls to $15.3 billion and Amgen and Horizon is the largest deal again. ANALYSIS

BLUE TEAM: "I&I IS WHERE THE MONEY IS GOING"

2026 is the largest I&I year in our count by value, and I&I leads listed-target value this year. VERIFIED **The counter:** it is one deal. The medians are flat across areas, 2025 had one I&I deal, and oncology led 2023. A second large I&I purchase before mid-2027 (call S1) would support the thesis; none would weaken it. ANALYSIS

SECTION	MAIN CLAIM	STRONGEST COUNTER-CASE	WHAT WOULD SETTLE IT
2 · Ledger	26 deals, Insmed the largest	The edge cases: count Alexion and Blueprint and the totals change, though Insmed still ranks first	A shared industry definition; we print ours and the edge list
3 · Areas	Typical deal size is similar across areas	Listed targets only; private deals, common in I&I, are left out	Adding private deals once their upfronts are confirmed
4 · Patterns	Approved drugs take the value	Four deals make most of it; with 26 rows, one deal moves every share	More years of data, or the same pattern in oncology
5 · China	China-sponsored trials rose from 7.5% to 37.9% of new I&I trials	Registry counts measure activity, not quality; many Chinese trials are small, China-only and may not read through to Western patients	Phase 2 and 3 results in Western trials, starting with HSK31858 and the bispecifics in the table
6 · What to track	The companies guide to a close in the first half of 2027	The largest deal in the ledger, with foreign reviews; Horizon took 298 days	The HSR outcome and the proxy timetable

Source note. SEC EDGAR: the merger agreements, 8-Ks, 6-Ks, 10-Qs and releases filed with them for every row (links in our figure list, available on request); Insmed 8-K of 11.24.2026, Exhibits 2.1 and 99.1; Drugs@FDA (NDA 217673); Sanofi, Merck, BMS, Pfizer and J&J annual reports via Mind Club's filings archive; external reference from the SEC sample of merger timelines in Mind Club's filings archive. Production: Mind Club research is developed through a human-led AI workflow using specialized expert agents, cross-model analytical challenge, primary-source review and substantial editorial direction. Independent analytical perspectives are used to test assumptions, identify weaknesses and refine conclusions. The human editor retains responsibility for the final work product.
Counted: 401 figures in our figure list behind this desk: 154 verified at the primary source tonight, 218 our own counts or sums built from those rows, 12 company statements of their own dates or plans, 3 external reference figures (labeled), 11 labeled Claim, and 3 not classified in the figure list. No outside estimate is used as a figure.

05 / FIVE TALKING POINTS — WHAT TO SAY ABOUT TODAY

FIVE TALKING POINTS

1. Sanofi's $41.0 billion offer for Insmed is the largest of 26 I&I acquisitions in our count since 2019 (see 04S). ANALYSIS
2. FDA approved Ekitna with sunitinib for GIST after imatinib, six days early; overall survival was not mature. VERIFIED
3. Medicare's 2028 Advantage and Part D rule is open for comment until 01.19.2027. VERIFIED
4. Moving antibiotics into the ambulance did not lower sepsis deaths in a randomized trial of more than 2,000 patients. VERIFIED
5. Povetacicept's 11.30 goal date is the only FDA date left in our two-week calendar. VERIFIED

05B / CLAIM CHECK — HEADLINE VS REGISTERED PROTOCOL

CLAIM CHECK

Five results checked against their registry records today. PEAK and PITSTOP's fluids comparison report their registered primaries. PITSTOP's antibiotic paper reports the registered primary but more patients than its record lists; DiaMedica's headline measure is not its registered primary; Avenzo's early data can't be judged yet.

READOUT	WHAT THE REGISTRY OR PRIMARY SOURCE SAYS	WHAT THE HEADLINE SAYS	VERDICT
Ekitna (bezuclastinib) · Cogent PEAK · NCT05208047	Phase 3. Part 2 primary: progression-free survival, about 48 months. N=482 (estimated, all parts); recruiting; primary completion 09.30.2025 (actual).	Median progression-free survival 16.5 vs 9.2 months with sunitinib alone (hazard ratio 0.50; 413 patients, per FDA)	MATCH
Ceftriaxone in the ambulance · PITSTOP NCT03068741	Phase 4. Primary: death before hospital discharge to day 90. N=2,061; completed; primary completion 11.17.2025.	Hospital mortality 18.0% vs 18.4% with placebo (2,091 randomized)	PARTIAL
Liberal fluids · PITSTOP NCT03068741	Same record and primary as above.	Hospital mortality 18.0% vs 18.3% with usual care (1,686 randomized, consistent with the factorial design)	MATCH
DM199 · DiaMedica NCT06875141	Withdrawn as entered in error; names a Pan African registry record, which we did not open. Primary listed: treatment adverse events.	9 of 10 with known delivery dates stayed pregnant past the historical median; no serious adverse events in 12	PARTIAL
AVZO-023 with fulvestrant · Avenzo ORION-1 · NCT06998407	Phase 1/2. Phase 1 primaries: dose-limiting toxicity and safety; Phase 2 primary: response rate. N=380 (estimated); recruiting; primary completion 08.2028.	Response rate 27% of 15 evaluable patients, per a secondary report; we could not open the company release	OPEN

Registry records from ClinicalTrials.gov, pulled 11.25.2026 REG; headlines from the sources cited in 04 and 08 CO PEER. A verdict says what differs, never why.

M&A, BD & LICENSING

A quiet day before Thanksgiving. We found no new acquisition, licensing, option or collaboration deal with stated terms in the window. The one item is a patent settlement that gives Amgen a dated U.S. launch for its Opdivo biosimilar.

BUYER	SELLER	ASSET OR MOA	AREA, STAGE	UPFRONT	TOTAL	
Amgen (11.24)	Bristol Myers Squibb and Ono (patent settlement, not a sale)	ABP 206, investigational biosimilar to Opdivo (nivolumab, anti PD-1 antibody)	Oncology, BLA under FDA review	Not disclosed; terms confidential	Not disclosed	SCAN

NOTES

Amgen says the settlement resolves the U.S. patent litigation over ABP 206 and that it will launch on 10.01.2028, subject to FDA approval. It says FDA is expected to act on the application by the end of 2026. VERIFIED

Sanofi and Insmed: the merger agreement is now filed; its fee, vote and end-date terms are in 04S, and 16 corrects yesterday's line on the break fee.

What we checked and did not find: no acquisition of an immunology and inflammation company or asset at $1.0 billion or more announced after 11.24; no acquisition of a biopharma company at $5.0 billion or more other than Sanofi and Insmed; no China-based company out-licensing ex-China rights with $100 million or more upfront. Pfizer's $330 million upfront in vivo CAR-T license from Starna Therapeutics was announced 11.18, outside this window. ANALYSIS

What pharma is willing to pay for. With no priced deal in the window, the clearest signal sits in capital markets: DiaMedica says a top five global pharma company bought into its $86 million offering (see 07). Strategic equity in a public raise is a cheaper way to watch an asset than a license. Amgen's settlement shows the other currency, certainty on timing, though its terms are private. ANALYSIS

Amgen release, 8-K Exhibit 99.1 (11.24) CO; Insmed 8-K (11.24) GOV; Pfizer and Starna release via Business Wire on Finviz (11.18) CO. We searched SEC full-text filings for 11.24 and 11.25 and newswire coverage.

RED TEAM

Our sweep leans on SEC filings and U.S. wires. Private deals in China, Korea and Europe often surface a day late, and a holiday week can push announcements to Monday. A settlement with confidential terms can still carry payments or royalties we cannot see. ANALYSIS

07 / FINANCING & CAPITAL MARKETS

$5M OR MORE, ANNOUNCED IN THE WINDOW

FINANCING & CAPITAL MARKETS

DiaMedica priced an $86 million offering, with a top five global pharma company among the buyers, per the company. It is the one new financing we count. No biotech IPO priced.

COMPANY	AMOUNT	STRUCTURE	STAGE	INVESTORS	IMPLICATION
DiaMedica Therapeutics (Minneapolis, Nasdaq: DMAC), 11.24	$86.0 million gross	Underwritten offering, 10,750,000 common shares at $8.00, a 9% discount to the 11.23 close of $8.82; close expected 11.25 VERIFIED	Clinical stage; DM199, a recombinant form of the KLK1 protein, in preeclampsia and fetal growth restriction	Led by new healthcare-focused institutional investors; includes an investment from an unnamed top five global pharma company CLAIM	Funds DM199 work in preeclampsia and fetal growth restriction, per the use of proceeds.

The offering priced an hour after interim data from 12 participants in a single-arm Phase 2 (see 08, 09). The company says the cash runs into 2030 and is meant to fund a larger placebo-controlled Phase 2, subject to regulatory alignment. VERIFIED

Queue and layoffs. Alopexx filed an amended registration on 11.24 for a long-pending IPO: 3,000,000 shares at $10 to $12 on NYSE American, ticker ALPX VERIFIED . Reported, not counted: a Korean start-up, Threebrooks Therapeutics, reported a Series A of $5.6M to $6.3M in one Dealroom report, which gives both figures; we found no company release CLAIM . We found no new biotech layoff in the window.

CAPITAL MARKETS TEMPERATURE. Warm but thin. A day after Kymera's $1.75 billion raise, the window held one priced offering and one amended IPO registration. In one deal, a 9% discount and an unnamed big pharma buyer suggest investors still fund clinical stories with strategic interest attached, while the holiday calendar keeps volume low. ANALYSIS

DiaMedica pricing release, 8-K Exhibit 99.1 (11.24) CO; DiaMedica 424B5 prospectus supplement (11.24) GOV; Alopexx S-1/A (11.24) GOV; Threebrooks via Dealroom (11.24) PRESS.

RED TEAM

DiaMedica's release went out at 7:00 am Eastern on 11.24, just before our window opened, so it may read as old news to some readers. The pharma investor is unnamed, and its stake size is not disclosed, so its weight as a signal is unknown. Private rounds in Asia and Europe often surface late and may change this count on Saturday.

ANALYSIS

CLINICAL READOUTS

A quiet day for company data. The weight sits with two JAMA trials: giving sepsis patients antibiotics or extra fluids in the ambulance did not lower hospital deaths. Two small early readouts round it out.

DRUG · COMPANY	MOA	INDICATION · TRIAL	N	RESULT, AS STATED	VERDICT
Ceftriaxone, given by paramedics · PITSTOP investigators (Sunnybrook, CIHR funded)	Cephalosporin antibiotic, 1 g intramuscular	Suspected sepsis with fever and low blood pressure, in the ambulance; PITSTOP-Antibiotics, randomized, placebo controlled; NCT03068741	2,091 randomized; 2,048 eligible for the primary analysis	Hospital mortality 18.0% vs 18.4% on placebo (risk ratio 0.97, 95% CI 0.81 to 1.17; P = .77); all 17 secondary outcomes similar. VERIFIED	failure
Liberal prehospital fluids · PITSTOP investigators	Up to 2 L normal saline regardless of blood pressure	Same population; PITSTOP-Fluids, the trial's second factorial comparison; NCT03068741	1,686 randomized; 1,646 in primary analysis	Hospital mortality 18.0% vs 18.3% with usual care (risk ratio 0.98, 95% CI 0.80 to 1.20; P = .82); median 1,500 mL vs 500 mL given. VERIFIED	failure
DM199 (rinvecalinase alfa) · DiaMedica	Recombinant human tissue kallikrein-1 (KLK1)	Early-onset fetal growth restriction; Phase 2 Part 3, open label, single arm, one center in Cape Town; registered as PACTR202404895013782	12 (6 per dose cohort)	9 of 10 with known delivery dates stayed pregnant past the published historical median; no serious adverse events or hypotension. Released 6:00 am ET 11.24, just before our window opened, and not in yesterday's edition. VERIFIED	partial
AVZO-023 with fulvestrant · Avenzo Therapeutics	Oral selective CDK4 inhibitor	Heavily pretreated HR-positive, HER2-negative advanced breast cancer; Phase 1/2 ORION-1; NCT06998407	15 evaluable (23 dosed)	Response rate 27% overall and 4 of 8 at 100 mg twice daily; disease control 73%; no dose-limiting toxicity at 150 mg twice daily. We could not open the company release. CLAIM	partial

01 PITSTOP: early antibiotics and extra fluids in the ambulance did not lower sepsis deaths

KNOW IT

RESULT

In a 2 × 2 factorial trial run by four Ontario paramedic services, adults with suspected infection, fever and systolic pressure under 100 mm Hg got 1 g of intramuscular ceftriaxone or placebo, and liberal or usual fluids. Neither comparison moved the primary outcome, death before hospital discharge up to day 90: 18.0% vs 18.4% for ceftriaxone vs placebo, and 18.0% vs 18.3% for liberal vs usual fluids. Both papers were published in JAMA on 11.24. VERIFIED

MIND CLUB IS PUBLISHED BY TORPEDO PUBLISHING LLC

COMPARATOR

Placebo in the ambulance, with open-label antibiotics in the emergency department (92% of both arms got them, a mean of about four hours after paramedics arrived). For fluids, usual care gave fluids only when systolic pressure fell below 90 mm Hg. VERIFIED

SAFETY

The authors report infrequent adverse events in both fluid groups, including fluid in the lungs during transport. The antibiotic abstract reports no safety signal; full safety tables are in the papers. VERIFIED

STATISTICAL VS CLINICAL SIGNIFICANCE

Neither result is statistically significant. The confidence intervals still allow a modest benefit (a relative cut in deaths of up to about 19% for ceftriaxone and 20% for fluids) or a modest harm, so "no effect" is the most likely reading, not a proven one. In practice, an antibiotic dose about 3.5 hours earlier did not change deaths in this population. ANALYSIS

INTERPRETATION

This is a large, randomized test of the "every hour counts" idea for antibiotics in sepsis, and it did not find a survival gain from moving the first dose into the ambulance. It may push health systems to question paramedic sepsis protocols. It is not a drug-development readout: ceftriaxone and saline are generic. ANALYSIS

REMAINING QUESTION

Whether a sicker subgroup, such as patients in septic shock, benefits from earlier treatment. A trial this size may not have the power to show that.

CLAIM CHECK PARTIAL NCT03068741 registers the same primary outcome (death before discharge to day 90). The record lists Phase 4 and enrollment of 2,061, while the antibiotic paper reports 2,091 randomized; the gap is not explained in the record.

02 DiaMedica's DM199 in fetal growth restriction: early, uncontrolled and small SCAN

RESULT

Twelve women with early-onset fetal growth restriction got DM199 under the skin every three days, at 5 or 10 µg/kg. Of 10 with known delivery dates, nine stayed pregnant longer than the published median expected time to delivery; three were still pregnant 22, 31 and 39 days after starting, against historical medians of 3 to 4 days. Doppler blood flow measures were "generally stable or improved" in several participants. Data cut-off was 10.13.2026. VERIFIED

COMPARATOR

None. Results are set against published historical medians, which included pregnancies with estimated fetal weight below the 10th centile; participants here were below the 3rd centile, per the investigator. VERIFIED

SAFETY

No serious adverse events, no hypotension, no treatment interruptions or discontinuations in 12 treated women, by the company's account. Two participants withdrew for social reasons. VERIFIED

STATISTICAL VS CLINICAL SIGNIFICANCE

No statistical test was reported. Longer pregnancy would matter clinically, since each week in the womb can matter for a growth-restricted baby, but a historical comparison in 10 women cannot show the drug caused it. ANALYSIS

INTERPRETATION

Early safety data worth watching in a condition with no approved drug, not evidence of efficacy. The company itself calls the findings preliminary and says randomized, controlled studies are needed. ANALYSIS

REMAINING QUESTION

Whether a randomized trial will follow, and with what endpoint: the registered primary is safety, not time to delivery.

CLAIM CHECK PARTIAL A ClinicalTrials.gov entry (NCT06875141) is withdrawn and names PACTR202404895013782 as the authoritative record; it lists treatment adverse events as the primary outcome. The headline measure, time to delivery against historical medians, is not the registered primary.

Scales et al., JAMA, 11.24.2026 (PITSTOP-Antibiotics) and JAMA, 11.24.2026 (PITSTOP-Fluids), via PubMed PEER; DiaMedica release (11.24, 6:00 am ET) CO; Avenzo results via TipRanks (11.24) PRESS; registry records NCT03068741, NCT06875141, NCT06998407 REG.

RED TEAM

PITSTOP was run in one Canadian province, and nearly every patient got antibiotics within hours anyway, so it tests a head start of about 3.5 hours, not antibiotics versus none. DiaMedica's 12-patient, single-center study has no control arm, and its comparison is to historical pregnancies that were less severely growth restricted, which could flatter the result either way. Avenzo's response rate comes from 15 patients on fulvestrant as well, so the share owed to CDK4 blockade alone is unknown, and we have only a secondary account of it. ANALYSIS

NOVEL BIOLOGY & TARGET WATCH

Two targets from today's small readouts: an old blood-flow enzyme, tissue kallikrein, now tried in the placenta, and CDK4 on its own, without CDK6. Neither has controlled proof of concept in people yet.

01 KLK1: can a kallikrein enzyme open up blood flow to a starving placenta? SCAN

TARGET

Tissue kallikrein-1 (gene KLK1), an enzyme of the kallikrein-kinin system that releases kinins, which raise nitric oxide and prostacyclin and relax blood vessels.

COMPANY

DiaMedica Therapeutics, with DM199 (rinvecalinase alfa), a recombinant form of the human enzyme given under the skin.

THESIS

In fetal growth restriction the placenta gets too little blood. DiaMedica's case is that DM199 may lower resistance in the mother's circulation and improve blood flow to the uterus and placenta, buying the baby time to grow. CLAIM

EVIDENCE

Interim results from the first two dose cohorts (six women each) of an investigator-sponsored, open-label, single-arm study at one South African hospital; two withdrew for social reasons. Of the 10 with known delivery dates, 9 passed the published historical median time to delivery, and Doppler measures were stable or improved in several. No serious adverse events or hypotension were reported. VERIFIED

VALIDATION STATUS

Hypothesis with early human safety data. There is no control arm, so the efficacy signal is not proof of concept. ANALYSIS

SIGNIFICANCE

Fetal growth restriction has no approved drug, so a blood-flow drug shown safe in pregnancy would fill a gap. A blood-pressure drop in the mother is the obvious worry with a vessel-relaxing enzyme, so the absence of hypotension in 12 women matters, if it holds. ANALYSIS

KEY QUESTION

Does a randomized trial show longer pregnancies and better outcomes for babies, not just for the pregnancy clock?

02 CDK4 alone: dropping CDK6 to spare the blood counts SCAN

TARGET

Cyclin-dependent kinase 4 (gene CDK4), a cell-cycle kinase that drives HR-positive breast cancer cells to divide. Approved drugs such as palbociclib block CDK4 and CDK6 together.

COMPANY

Avenzo Therapeutics, with AVZO-023, an oral CDK4-selective inhibitor, tested alone, with fulvestrant, and with its CDK2 inhibitor AVZO-021 in ORION-1 (NCT06998407).

THESIS

CDK6 matters for blood cell production, so blocking CDK4 alone may allow fuller tumor suppression with less neutropenia, the main side effect of today's drugs. ANALYSIS

EVIDENCE

Per a secondary report, 27% of 15 heavily pretreated patients responded on AVZO-023 with fulvestrant, with one Grade 3 drop in neutrophils at 100 mg twice daily and no dose-limiting toxicity at 150 mg twice daily. We could not open the company release. CLAIM

VALIDATION STATUS

Early clinical activity in a dose-finding study. Fulvestrant contributes on its own, and there is no comparator, so this is not proof of concept for CDK4 selectivity. ANALYSIS

SIGNIFICANCE

Several companies are chasing CDK4-selective drugs for patients whose cancer progressed on CDK4/6 inhibitors. Low blood-count toxicity at doses that shrink tumors would be the point of difference. ANALYSIS

KEY QUESTION

Do responses hold in patients who already progressed on a CDK4/6 inhibitor, and at what neutropenia rate once more patients are dosed?

DiaMedica release (11.24) CO; Avenzo results via TipRanks (11.24) PRESS; NCT06998407 and NCT06875141, pulled 11.25.2026 REG.

Target Evidence Card: KIT

KIT scores 0.91 for genetic association with gastrointestinal stromal tumor in Open Targets. Eighteen active trials test drugs aimed at KIT alone, five of them in Phase 3 and two in GIST. Ekitna (bezuclastinib), approved 11.24 with sunitinib, is the first FDA-approved drug we count as aimed at KIT alone.

HUMAN GENETICS

0.91

for gastrointestinal stromal tumor (MONDO_0011719), Open Targets genetic association, direct (overall 0.89; somatic mutation 0.78). Top elsewhere: cutaneous mastocytosis 0.92 and piebaldism 0.91, a pigment disorder; not support for this indication. Direction not established: no carrier or Mendelian randomization data pulled today. 2,707 associations in all.

MECHANISM

Receptor kinase

Receptor for stem cell factor that sends cell survival and growth signals. Class from Open Targets (kinase, PDGFR family); ChEMBL had no curated mechanism for bezuclastinib on 11.25.2026.

HOW CROWDED

18

active interventional trials on ClinicalTrials.gov (recruiting, not yet recruiting, active not recruiting, enrolling by invitation; all diseases) of drugs aimed at KIT alone: barzolvolimab 6, briquilimab 5, bezuclastinib 4, NN3201 1, NN2802 1 and donor CD117 CAR-T cells 1. Two are in GIST (PEAK, and a Phase 2 after sunitinib). Phase 3 count: 5, with Phase 2/3 counted as Phase 3 (none among these). Comparator and backbone trials included (PEAK); background-only trials excluded. Plus 41 multi-target on 10.23.2026 (velzatinib, avapritinib, ripretinib and older KIT-active pills in GIST), not recounted today.

THE BAR

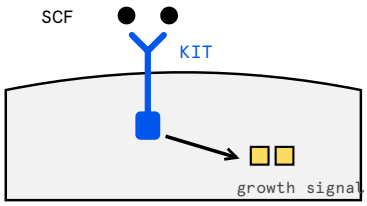
1

FDA-approved product, including biosimilars: Ekitna (bezuclastinib, Cogent), approved 11.24.2026 with sunitinib for adults with advanced GIST after imatinib; no biosimilars apply. Counted as aimed at KIT alone on selectivity data read 10.23.2026; not yet in openFDA on 11.25.2026. Not counted, as each also hits other kinases: Gleevec (NDA 021588), Ayvakit (NDA 212608), Qinlock (NDA 213973) and Rydapt (NDA 207997), each marketed per openFDA, plus broad multi-kinase drugs such as sunitinib.

HOW IT WORKS

Think of KIT as a gas pedal on a cell. In GIST a mutation jams it down and the tumor grows. When imatinib stops working, bezuclastinib joins sunitinib to try to ease the pedal from a second angle.

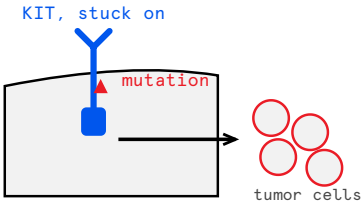
1 · THE GAS PEDAL



KIT is a receptor kinase. When stem cell factor binds it, KIT sends signals that keep cells alive and growing.

DEMONSTRATED

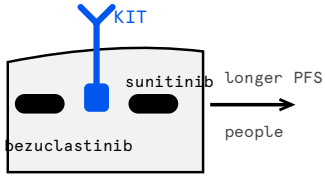
2 · JAMMED DOWN



KIT-mutant GIST is driven by activating changes in KIT, and tumors on imatinib often relapse as cells with new resistance mutations grow out. KIT scores 0.91 for GIST genetic association.

SUGGESTIVE

3 · TWO PILLS, ONE TARGET



Bezuclastinib, which a peer-reviewed trial paper by its developers calls a highly selective KIT inhibitor, is taken with sunitinib. In the randomized, open-label PEAK trial, the pair lengthened median progression-free survival (hazard ratio 0.50).

DEMONSTRATED

Solid: seen in people (any design, including genetic association). Dashed: animals or cells. Dotted: hypothesis or company claim. Line style shows where a step was seen, not proof.

EVIDENCE LADDER

DEMONSTRATED	In the randomized, open-label PEAK trial (413 patients with advanced GIST after imatinib), bezuclastinib plus sunitinib lengthened median progression-free survival to 16.5 months from 9.2 months on sunitinib alone (hazard ratio 0.50), and the FDA approved the pair on 11.24.2026; overall survival was not mature.
SUGGESTIVE	In a nonrandomized Phase 1b/2a study of bezuclastinib (then called PLX9486), 39 patients in all, the GIST group that took it with sunitinib, a drug that binds KIT in a different shape, showed clinical benefit. KIT scores 0.91 for GIST genetic association.
SPECULATIVE	That the progression-free gain turns into longer overall survival, which was not mature at the PEAK analysis, and that the liver risk behind the boxed warning stays manageable outside a trial.

Who's running. Cogent (bezuclastinib: PEAK, the Phase 3 behind the approval, still listed as recruiting; SUMMIT and APEX, Phase 2 in systemic mastocytosis), the Sarcoma Alliance for Research through Collaboration (bezuclastinib plus sunitinib after sunitinib, Phase 2), Celldex (barzolvolimab: three Phase 3 trials and a Phase 3b extension in urticaria), NIH and academic centers (briquilimab in transplant conditioning) and Novelty Nobility (NN3201, a c-Kit antibody-drug conjugate, Phase 1 in solid tumors including GIST; NN2802, an anti-c-Kit antibody, Phase 1/2 in urticaria, recruiting since 10.15.2026). GSK's velzatinib, in a Phase 3 against sunitinib after imatinib (StrateGIST 3), is counted as multi-target. Some records may be stale: PEAK and APEX list primary completion dates in 2025 but still read recruiting. Blueprint's BLU-808 urticaria trial now reads completed. VERIFIED

V1 · 10.23.2026	V2 · 11.25.2026	NEXT RE-PULL
Library card, not printed; headline 18, bar 0	Rebuilt for GIST: bar 0 to 1 (Ekitna); headline 18 and Phase 3 5 hold	On next lead mention or after 90 days

Open Targets Platform: KIT target record and associations, release 26.09, 11.25.2026 DATA. ChEMBL CHEMBL5095229 (bezuclastinib; no curated mechanism), 11.25.2026 DATA. ClinicalTrials.gov search by drug name (barzolvolimab, CDX-0159, briquilimab, JSP191, bezuclastinib, CGT9486, PLX9486, elenestinib, BLU-263; BLU-808, IDRX-42, velzatinib, NB003, c-kit, CD117), 11.25.2026, interventional, active statuses: NCT06727552, NCT06455202, NCT06445023, NCT07266402, NCT06366750, NCT07256392, NCT05357482, NCT05600907, NCT06145282, NCT05907746, NCT04784052, NCT06208748, NCT05186753, NCT04996875, NCT05208047, NCT06805825, NCT07930572, NCT07144020, and NCT07218926 (velzatinib) and NCT06931405 (BLU-808, completed) REG. FDA on bezuclastinib (PEAK results, boxed warning) and openFDA Drugs@FDA records (Gleevec, Ayvakit, Qinlock, Rydapt; no bezuclastinib record yet), 11.25.2026 GOV. Wagner et al., JAMA Oncology, 2021 (PLX9486 with sunitinib, nonrandomized Phase 1b/2a, 39 patients), via PubMed PEER.

BLUE TEAM · THE CASE

Adding a selective KIT inhibitor to sunitinib may be worth having in GIST after imatinib even before survival data arrive. In the randomized PEAK trial, the pair lengthened median progression-free survival to 16.5 months from 9.2 months (hazard ratio 0.50), and KIT scores 0.91 for GIST genetic association. The thesis would strengthen if overall survival, not yet mature, favors the pair and liver safety holds in routine use. ANALYSIS

RED TEAM · THE CATCH

PEAK was open-label and compared the pair with sunitinib alone, so it shows a progression-free gain over one older drug, not over other options after imatinib. Overall survival was not mature. The label carries a boxed warning for liver toxicity. Bezuclastinib's selectivity rests on its developers' own papers and posters, and GSK's velzatinib is in a Phase 3 against sunitinib in the same setting. ANALYSIS

POLICY & REGULATORY WATCH

FDA approved Cogent's GIST drug six days early, and CMS opened its 2028 Medicare Advantage and Part D rulemaking. Povetacicept is still pending ahead of its 11.30 goal date.

ITEM	STATUS	WHAT HAPPENED	WHAT IT COULD MEAN
FDA (11.24): Ekitna (bezuclastinib) with sunitinib	Approved	Approved for adults with advanced GIST after imatinib, the 57th entry on FDA's 2026 novel approvals list. In the PEAK trial (413 patients), median progression-free survival was 16.5 months vs 9.2 months on sunitinib alone (hazard ratio 0.50). Boxed warning for liver toxicity. Overall survival was not mature. VERIFIED	Action came ahead of the 11.30 goal date. Cogent says the drug is available now. Cogent's nonadvanced systemic mastocytosis application has a 12.30.2026 goal date, and its advanced systemic mastocytosis application 06.29.2027, per its third quarter 10-Q.

ITEM	STATUS	WHAT HAPPENED	WHAT IT COULD MEAN
FDA: povetacicept (Vertex) in IgA nephropathy	Under review	No action found. The drug is not on FDA's novel approvals list as of 11.24, and Vertex has filed no 8-K since 11.02. Its third quarter 10-Q gives a goal date of 11.30.2026 under priority review for accelerated approval. VERIFIED	A decision may come on or before Monday. A miss on the date would be news in itself.
CMS (11.25): contract year 2028 Medicare Advantage and Part D rule	Proposed	Published in the Federal Register. It covers marketing, drug coverage, enrollment and special needs plans, and would set up a mandatory Medicare Advantage model at the CMS Innovation Center. Comments close 5 p.m. ET, 01.19.2027. VERIFIED	Part D coverage terms for 2028 are in play. We have the abstract only; drug provisions need a full read before we say more. A companion rule, CMS-4214-P (Part D low-income cost sharing, provider directories and PBM accountability), was published 10.20.2026; its comments close 5 p.m. ET, 12.15.2026. VERIFIED
CMS: Medicare negotiation, fourth cycle	Proposed	CMS's selected drug page, last modified 11.23, lists drugs for 2026 to 2028 only. No list for 2029 is posted. VERIFIED	The next selection, the second to include Part B drugs, is still ahead.
FDA (11.25): OTC monograph order requests	Guidance	Guidance for industry on the format and content of over-the-counter monograph order requests, noticed in the Federal Register. VERIFIED	Process detail for consumer health sponsors; little read-through to drug development.
White House / Senate: FDA Commissioner	Political	We found no new nomination since Heidi Overton's was withdrawn on 11.17. We could not open congress.gov this morning, so this rests on news searches. CLAIM	FDA may stay without a confirmed commissioner into the new Congress.

MEDICARE ACCESS WATCH

A quiet week for Part B drug coverage. Nothing national or local in the last seven days names a drug or biologic; the three national postings are device and procedure items.

DATE	DOCUMENT	WHAT CHANGED	READ
11.23	NCD 20.32, transcatheter aortic valve replacement (TAVR)	New version posted, effective 09.10.2026	SCAN
11.18	NCA CAG-00471N, leadless cardiac resynchronization (WiSE)	Proposed decision memo posted; analysis open	KNOW IT
11.18	NCA CAG-00060R2, hyperbaric oxygen for radiation proctitis and enteritis	New tracking sheet; reconsideration open	SCAN
11.13	Local article A52451, ranibizumab, aflibercept and biosimilars (Wellpoint Federal)	Billing and coding update. The latest drug item in the local report; no local postings after 11.13	SCAN

FDA Novel Drug Approvals 2026; FDA on bezuclastinib; Federal Register, CMS proposed rule; Federal Register, OTC guidance; CMS selected drugs; CMS Medicare Coverage Database, national report for the past 7 days and local report, pulled 11.25.2026 GOV; Cogent release; Vertex third quarter 10-Q CO; Healio on the Overton withdrawal PRESS. Coverage tools hold Part B (NCDs and LCDs) only; Part D formularies aren't in that database.

RED TEAM

FDA's advisory committee calendar page was empty when we read it, and congress.gov would not load, so an advisory meeting or a nomination could be missing. We read only the abstract of the CMS rule. The local coverage report would not filter by date, so we relied on its default listing. ANALYSIS

PATTERN RECOGNITION

Two early actions this week. Ekitna was approved six days before its goal date, after BridgeBio's Welgemda came four days early on 11.23. Two cases in two days is not a policy, but it is worth watching before povetacicept's 11.30 date. ANALYSIS

Approved drugs draw the money. Sanofi is paying for a launched drug, and the 04S ledger shows approved assets taking most of the I&I deal value since 2019 while Phase 2 assets make up much of the count. ANALYSIS

Pharma as investor, not buyer. A top five pharma company bought into DiaMedica's offering rather than licensing the drug. One case, not yet a pattern. ANALYSIS

WHAT MAY BE UNDERESTIMATED

Survival is still open for Ekitna. The approval rests on progression-free survival, with overall survival not mature and a boxed liver warning. Use outside the trial may show how much the liver risk weighs against months without progression. ANALYSIS

WHERE THIS BRIEF COULD BE WRONG

Our biggest conclusion, the strongest case against it, and what would settle it.

RED TEAM

Base case. Sanofi is buying an approved lung drug with room to grow, and the deal tops our I&I count. ANALYSIS

Counter-case. Brinsupri has been on the U.S. market only since August 2025, rivals are in Phase 3, and how we define I&I decides the ranking: bronchiectasis sits at the edge of classic immunology, and a wider or narrower definition would change the count.

What would settle it. Brinsupri's sales over the next year, and the ledger's ranking under the definitions printed in 04S.

CONSENSUS	COUNTER-CASE	WHAT WOULD SETTLE IT
Ekitna improves outcomes in GIST after imatinib	The gain is in progression-free survival; overall survival was not mature, and the label warns of liver toxicity	PEAK's overall survival analysis
Earlier antibiotics do not help sepsis patients in the ambulance	The confidence interval allows a relative cut in deaths of up to about 19%, and sicker patients may differ	Subgroup data and other prehospital trials
A top five pharma investment signals interest in DM199	An equity stake commits no development money, and the data are uncontrolled in 12 women	A controlled trial or a licensing deal

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BLIND SPOT CHECK

Newswire feeds were partly blocked to our tools, so we searched SEC filings and web results instead; a late release may be missing. We read only the abstract of the CMS rule. Congress.gov would not load, so the FDA Commissioner item rests on news searches. FDA's advisory committee calendar read as empty, which may be a page problem. Avenzo's data rest on a secondary report. The FedWatch reading is secondhand. ClinicalTrials.gov, Open Targets, ChEMBL, PubMed and the CMS coverage database were reached through their connectors.

14 / VERIFIED CATALYST CALENDAR WED 11.25 TO WED 12.09 · EVERY DATE GRADED

VERIFIED CATALYST CALENDAR

Vertex's povetacicept goal date on 11.30 is the one FDA date left in the window; Cogent's, set for the same day, is done. Then CHMP, the FOMC, SABCS and the run-up to ASH. Six of 7 dates are confirmed at the source; the seventh is a registry estimate.

DATE	EVENT	WHO	CONFIRMED AT
Mon 11.30	Goal date, povetacicept in IgA nephropathy (accelerated approval, priority review); no FDA action found as of 11.25	Vertex	COMPANY
Mon 12.07 to Thu 12.10	CHMP meeting	EMA	GOV
Tue 12.08	Estimated primary completion, LIBREXIA-AF (milvexian vs apixaban in atrial fibrillation, about 20,300 patients); status active, not recruiting; no topline posted	Johnson & Johnson	REGISTRY
Tue 12.08 to Wed 12.09	FOMC meeting, with economic projections	Federal Reserve	GOV
Tue 12.08 to Fri 12.11	San Antonio Breast Cancer Symposium	SABCS	ORGANIZER
Wed 12.09	ASH virtual platform opens to attendees	ASH	ORGANIZER
Sat 12.12 to Tue 12.15	ASH Annual Meeting, New Orleans (just past the window)	ASH	ORGANIZER

Grades: Company, Gov and Organizer mean we opened that source this morning; Registry means an estimated date in ClinicalTrials.gov, which sponsors can move. Company sources: Vertex third quarter 10-Q and Vertex release (06.01) CO; EMA; Federal Reserve FOMC calendar GOV; ClinicalTrials.gov NCT05757869, updated 11.03 DATA; AACR on SABCS and American Society of Hematology CO. Cogent's 11.30 GIST date is gone: FDA acted on 11.24. Comments on CMS's 2028 Medicare Advantage and Part D proposal close 01.19.2027, outside this window. FDA's advisory committee calendar showed no meetings when we read it. Calendar dates can move without notice.

14B / REGISTRY WATCH 70 TRIALS · PULLED 11.25 · CHANGES ONLY

RIBOCURE'S VORTOSIRAN AF TRIAL IS NOW RECRUITING

All 70 watchlist trials were pulled today. One changed since 11.24: the Phase 2b of vortosiran in atrial fibrillation moved from not yet recruiting to recruiting, and its start date moved from 10.01.2026 to

10.15.2026. No other trial changed in status, enrollment, primary outcome, phase, dates or results. SAFFRON, due to complete 11.23, still reads active, not recruiting. The full table returns Friday.

TRIAL	LABEL	FIELD	WAS	NOW	WHAT IT MAY MEAN
NCT07870889	**Vortosiran AF Ph2b (Ribocure)**	Status	NOT_YET_RECRUITING	RECRUITING	The record, updated 11.24, now lists an actual start; enrollment of 150 and primary completion of 07.31.2028 remain estimates.
NCT07870889	**Vortosiran AF Ph2b (Ribocure)**	Start date	2026-10-01	2026-10-15	The registry now marks the start as actual, two weeks later than the earlier date.
NCT05261399	**SAFFRON**	Completion date passed	Due 11.23.2026	Still active, not recruiting	The record, last updated 08.06, may simply lag; a change to completed, or a new date, would show whether the study ended on time.

ClinicalTrials.gov watchlist, pulled 11.25.2026 through the registry's API REG: 70 trials, 70 pulled, 0 failed. Compared with the 11.24 pull on status, enrollment, primary outcome, start, primary completion, completion, phase and results flag.

PUBLIC CALLS LEDGER

Ten new calls open today, from FDA's povetacicept decision to the next large I&I purchase. No call resolved since the last edition. The time-weighted score across 17 resolved calls is 0.121.

OPEN CALLS

#	CALL	OUR ODDS	RESOLVES BY	BASE RATE	RESOLUTION SOURCE
18 (B1 in 04S)	FDA approves Vertex's povetacicept for IgA nephropathy (any approval, accelerated included), as shown on Drugs@FDA, on or before 12.07.2026. Goal date 11.30.2026.	80%	12.07.2026 ET	83%: our FDA approval calls, 5 of 6 approved by the date	Drugs@FDA (fallback: Vertex release)
19 (B2 in 04S)	Insmed files a preliminary proxy statement (Form PREM14A) for its merger with Sanofi on SEC EDGAR on or before 12.18.2026.	90%	12.18.2026 ET	Too few: n=1	SEC EDGAR, Insmed filings
20 (B3 in 04S)	A biopharma company announces a definitive agreement to acquire another biopharma company with a stated total transaction value of $5.0 billion or more, excluding Sanofi and Insmed, between 11.25.2026 and 01.15.2027.	65%	01.15.2027 ET	Too few: n=1	The buyer's release (fallback: SEC 8-K)
21	Bristol Myers Squibb or Johnson & Johnson announces topline results of the LIBREXIA-AF Phase 3 of milvexian (NCT05757869) on or before 01.15.2027.	20%	01.15.2027 ET	Too few: n=2	BMS newsroom (fallback: J&J newsroom)

#	CALL	OUR ODDS	RESOLVES BY	BASE RATE	RESOLUTION SOURCE
22	ClinicalTrials.gov lists BMS-986553 study NCT07873931 (refractory autoimmune diseases) as Recruiting on or before 01.15.2027.	55%	01.15.2027 ET	Too few: n=2	ClinicalTrials.gov record NCT07873931
23	CMS publishes the list of drugs selected for negotiation for initial price applicability year 2029, and the list includes at least one drug payable under Medicare Part B, on or before 02.01.2027.	85%	02.01.2027 ET	Too few: n=1	CMS selected drugs page (fallback: CMS release)
24	At least two licensing or option deals in which a China-based company grants rights outside China to a non-Chinese biopharma company, each with $100 million or more paid up front, are announced between 11.25.2026 and 01.15.2027.	75%	01.15.2027 ET	None found: no resolved call on this count	The licensee's release for each deal (fallback: HKEX filing)
25	The President sends the Senate a new nomination for Commissioner of Food and Drugs, as recorded on Congress.gov, between 11.25.2026 and 01.15.2027.	20%	01.15.2027 ET	None found: no resolved nomination call	Congress.gov nominations (fallback: White House)
26	FDA publishes a Federal Register notice of an advisory committee meeting to discuss uniQure's AMT-130 BLA in Huntington's disease on or before 01.15.2027.	25%	01.15.2027 ET	None found: no resolved advisory committee call	Federal Register (fallback: FDA advisory calendar)
27 (S1 in 04S)	A biopharma company announces a definitive agreement to acquire an I&I company or I&I lead asset, as our Special Coverage desk defines it, with a stated value of $1.0 billion or more, between 11.25.2026 and 03.31.2027.	65%	03.31.2027 ET	68%: our I&I deal ledger's pace, 26 deals since 2019 (Poisson)	The buyer's release (fallback: SEC 8-K)

Tests in brief. 18: a complete response letter, or a goal date moved past 12.07, is no. 19: other proxy forms, such as soliciting material, do not count; the merger agreement asks for the preliminary proxy within fifteen business days of 11.23. 20 and 27: a signed definitive agreement only; licenses, options and reports do not count; contingent value counts only if the upfront alone clears the line. One deal can resolve both. 21: a registry change alone does not count. 22: only the registry status counts. 24: undisclosed upfronts and acquisitions do not count. 25: a named pick without a transmitted nomination is no. 26: a company statement without the notice is no. Next dated facts for the calls between 35% and 65%: the J.P. Morgan Healthcare Conference, 01.11 to 01.14.2027 (20 and 27); the registry's next update for NCT07873931, whose estimated start of 10.30.2026 has passed (22). Benchmark: we found no Kalshi or Polymarket market on any of these ten events on 11.25.2026. Seed checks were run on 11.25.2026; none of the events has happened. FORECAST

RESOLVED SINCE THE LAST EDITION

None. All 17 earlier calls are resolved and were printed with their results.

RUNNING RECORD

MEASURE	SCORE
Resolved calls	17

MEASURE	SCORE
Brier, time-weighted (headline)	0.121
Brier, last odds	0.107
Brier, first odds	0.130
Beat their base rate	Not graded

From this edition our calls follow a written standard: one dated proposition, one named resolution source, stated odds and a base rate where one exists. Calls 9, 10 and 12 are clarified: source named, test unchanged. Call 8 was first printed at 70%, not 50%; the ledger history is corrected.

#	CLARIFIED WORDING	RESOLUTION SOURCE
09	A definitive agreement to acquire a biopharmaceutical company, or a drug program, with a stated upfront value of $5.0B or more is announced between 10.01.2026 and 12.31.2026.	The buyer's press release
10	CMS publishes the negotiated maximum fair prices for the 15 drugs selected for initial price applicability year 2028 (the IRA's third cycle) on or before 11.30.2026.	CMS drug price negotiation program page
12	FDA approves BridgeBio's BBP-418 for limb-girdle muscular dystrophy type 2I/R9 on or before 11.27.2026.	BridgeBio news releases (fallback: FDA approval letter)

Brier score = (our probability minus outcome) squared; 0 is perfect and 0.25 is what always saying 50% earns. The time-weighted score averages each call's odds over the days it was open. Base rates are our own counts of resolved calls of the same kind, except call 27, which uses our desk's deal count. None of our resolved calls carried a base rate, so none is graded against one. Calls cover scientific, regulatory, policy and deal events only, never share prices. Sources: ClinicalTrials.gov NCT05757869 GOV; ClinicalTrials.gov NCT07873931 GOV; Sanofi and Insmed merger agreement, Section 5.2 REG; CMS selected drugs page GOV; CMS negotiation milestones GOV.

ASK MIND CLUB AND CORRECTIONS

Two corrections to Edition 055 on the Sanofi and Insmed deal, both rechecked at the SEC filings. The full log of 19 corrections is on the track record page.

EDITION	WE SAID	THE RECORD SHOWS
055 (11.24)	In 06 M&A, BD & licensing: "The deal can still fail on the vote or in review, and terms say nothing yet about a break fee."	The merger agreement sets a $1.125 billion termination fee payable by Insmed to Sanofi in specified cases (Section 7.3(b)). It sets no fee payable by Sanofi. Insmed can instead seek specific performance, that is, ask a court to force the deal through (Section 8.6(b)). VERIFIED
055 (11.24)	In 06: "Most of the price rests on one drug, which the companies say brought in $1.09 billion through 09.30.2026, its first full year on the market." In 13 Where this brief could be wrong: "Brinsupri is in its first full year".	The companies say Brinsupri brought in $1.09 billion following its U.S. launch in August 2025 through 09.30.2026, more than 13 months and longer than a first full year. FDA approved it on 08.12.2025. The release does not split the figure by country. VERIFIED

Sources: Agreement and Plan of Merger, Insmed 8-K Exhibit 2.1 (11.24) REG; Sanofi and Insmed joint release, Exhibit 99.1 (11.24) CO; Drugs@FDA, NDA 217673 GOV.

SOURCES

1. Company releases and filings: Sanofi and Insmed (Insmed 8-K and exhibits), Cogent, DiaMedica, Amgen, Pharming, Alopexx, Vertex (third quarter 10-Q), and the acquirers' releases and filings behind the 04S ledger CO
2. FDA announcements and Novel Drug Approvals 2026; Federal Register; CMS selected drugs page and Medicare Coverage Database; EMA CHMP calendar; U.S. Treasury daily par yield curve; FOMC calendar GOV
3. Robinhood market data (11.24 closes) DATA
4. ClinicalTrials.gov: NCT05208047, NCT03068741, NCT06875141, NCT06998407, the 70-trial watchlist and the KIT trial search for the card REG
5. JAMA papers via PubMed and DOI PEER
6. Open Targets, ChEMBL and Drugs@FDA for the Target Evidence Card DATA
7. CappNotes, Healio, TipRanks, Dealroom, StockTitan PRESS

Every source above was opened by the run that built this edition or its research lanes, except where an item says it was not.

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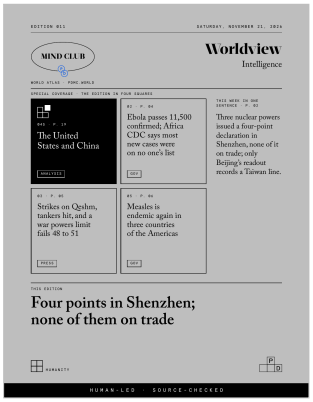
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