BofA SECURITIES

US Biopharmaceuticals

Our day 2 conference takeaways: INSM, ESPR, and KURA

Price Objective Change

Summarized below are our takes from today's presentations and management meetings...

INSM: Confidence high ahead of likely transformative year

Following Monday's presentation (see our Day 1 takes), management re-emphasized the potential of its three near-term pillars, with peak guidance of >$1B for Arikayce, >$5B brensocatib, and >$2B for TPIP—upside we've long thought underappreciated. To be fair, we suspect confidence in Arikayce has grown on the back of the solid 1L data (see our ARISE takes), but we wouldn't be surprised if skepticism remains for brensocatib with TPIP largely off most investor radars. On the former, we were encouraged by the team's messaging and tone, both on the ASPEN readout (2Q) as well as the multiple paths to potential approval. Indeed, while declining to provide an updated blended exacerbation rate (1.12-1.15 prior), Insmed stressed the numbers remain "in the neighborhood", well below the 1.37 placebo from the phase 2 WILLOW. Together with the study's powering assumptions, we see reasons to be optimistic ASPEN can demonstrate an improvement well above the 15% threshold management believes necessary to be commercially viable. At the same time, Insmed remains heartened by the initial TPIP PH-ILD/ PAH data, especially given interest in raising the dose ceiling with PAH to 1,280µg, with treprostinil's benefit clearly correlated to exposure—and we could see potential for greater appreciation of the molecule's upside if the PH-ILD update (2Q) match the early insights (see our TPIP takes). On the regulatory front, Insmed continues to work with the FDA's PRO group to align on ENCORE's endpoints, setting up a potential 1L approval for 2026—though the team admitted there was a low chance they may be able to file on ARISE. Ultimately, with all three pillars looking well-positioned to deliver, we continue see solid risk/ reward for shares; Maintain Buy and $37 PO.

ESPR: With litigation addressed, focus pivots to relaunch

While absent much new insight, we liked management's tone during this afternoon's presentation, where the team provided FY24 OpEx guidance of $225-$245M. During our in-person discussions though, they continued to highlight the benefits of the settlement with DSE (see our takes on the resolution). To be fair, we wouldn't be surprised if many investors were initially disappointed by the $125M payment, meaningfully lower than the original $200-300M milestone. Still, we think the deal made sense given the NT capital needs, removing a potential distraction ahead of the US re-launch (CLEAR label update PDUFA: Mar 31st)—even as some other components of the deal weren't as immediately apparent (i.e., savings on manufacturing and potential of a triple combination in the EU to extend the patent life). Rather, our concern has been the LT commercial opportunity for bempedoic acid (BA) and its ability to capture share likely positioned after generic statins but before more effective PCSK9s. We certainly don't doubt BA has a place in the paradigm, but with our KOLs pointing to the many clinical, logistical, and financial challenges of getting patients on lipid lowering therapies to begin with, pressured by the growing competitive landscape, we are currently more cautious on the opportunity. Reiterate Neutral but increase our PO to $2.80 (from $2.50 prior) given our adjustments to better account for savings associated with the DSE deal. *<continued on page 2>*

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Equity
United States
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Abbreviations:
TPIP: treprostinil palmitil inhalation powder
PAH: pulmonary arterial hypertension
PH-ILD: pulmonary hypertension with interstitial lung disease
PRO: patient reported outcome
NT: near-term
LT: long-term
PSCK9: proprotein convertase subtilisin/ kexin type 9
KOLs: key opinion leaders
BA: bempedoic acid
PDUFA: Prescription Drug User Fee Act
1L: frontline
FDA: Food and Drug Administration
DSE: Daiichi Sankyo Europe

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KURA: '007 front and center, with fuller combo picture YE

We thought management did a solid job framing Kura's development strategy and the NT clinical updates—with (in our view), 2024 shaping up to be a pivotal year for both the company and the menin inhibitor class. Indeed, with sentiment on the MoA improving on the back of solid ASH updates from rival Syndax (our takes on Monday's presentation), we think investors are rapidly pivoting focus to the opportunities in earlier line settings, which will almost assuredly require combination approaches. Here, Kura's KOMET-007 (data expected Jan/ Feb) is shaping up to be the next key catalyst, with the team reiterating plans to share data from ~20 patients across the four cohorts (i.e., "7+3" and ven+aza in both *KMT2Ar* and *NPM1*m AML subtypes) with ~2-3 cycles of therapy at the 200mg dose—with a second, more in-depth look planned at EHA (June 13-16). That said, we think the NT update should provide meaningful insights into the combination safety profile, specifically rates of DS, DDIs, and myelosuppression and how they compare to SoC levels. At the same time, management categorized a win on efficacy as a 50-70% CR rate for the 7+3 + zifto combo and 30-40% CR/CRis in ven + aza + zifto regimen. Longer-term, Kura guided to data from KOMET-008—its combo study with LDAC, FLAG-IDA, and gilteritinib in R/R AML—and the post-transplant maintenance study (KOMET-012) at ASH (Dec 7-10). Ultimately, with a sound clinical strategy supporting multiple NT catalysts capable of driving a re-rating, we continue to see upside to shares at current levels. Maintain Buy and $31 PO.

Abbreviations:

MoA: mechanism of action
ASH: American Society of Hematology
KMT2Ar/ NPM1m: genotypes
AML: acute myeloid leukemia
DS: differentiation syndrome
EHA: European Hematology Association
DDIs: drug-drug interactions
CR/ CRi: complete response/ with incomplete count recovery
R/R: relapsed/ refractory
FLAG-IDA: Fludarabine, Cytarabine, Idarubicin and G-CSF
LDAC: low-dose cytarabine
YE: year-end
LT: long-term

Exhibit 1: Stocks mentioned
Prices and ratings for stocks mentioned in the report

BofA Ticker	Bloomberg ticker	Company name	Price	Rating
ESPR	ESPR US	Esperion	US$ 2.75	C-2-9
INSM	INSM US	Insmed	US$ 28.34	C-1-9
KURA	KURA US	Kura	US$ 15.09	C-1-9

Source: BofA Global Research

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Price objective basis & risk

Esperion (ESPR)

Our 12-month price objective (PO) is based on our NPV analysis of revenue forecasts and estimated margin assumptions. We forecast sales of bempedoic acid with a terminal growth rate of -50%, supplemented by updated milestones and ROW royalties with a terminal growth rate of -50%. Given a WACC of 9% in-line with similar commercial-stage biotechs, we estimate a PO of $2.80/ share.

Upside risks to our PO:
1) near-term label expansion to reflect CLEAR Outcomes, 2) strong support from (esp) community-based providers to broadly administer BA to patients, 3) expanded payer coverage, 4) robust adoption and growth OUS, supporting royalty growth and milestones, and 5) pipeline success, including an oral PSCK9 inhibitor and a next gen ACLY inhibitor.

Downside risks to our PO:
1) label expansion delays, 2) slow uptake among prescribers, especially those in community settings, 3) payer pushback, including poor formulary positioning and use restrictions, 4) underwhelming uptake OUS, limiting royalties/ collaboration milestones, 5) competition from other lipid modifying therapies, and 6) difficulties securing funding to support commercial and development activities.

Insmed Incorporated (INSM)
Our 12-month PO is based on our NPV analysis of revenue forecasts assumptions. We model sales of Arikayce for refractory NTM-PD and frontline expansion (modified by a LOS of 80%). We assume a collective value for the pipeline: Brensocatib in NCFB (LOS: 65%), with potential expansion into CF (LOS: 20%), CRSsNP, and HS (LOS: 15%) and TPIP for PAH and PH-ILD (LOS: 50%). Given a WACC of 15%, in line with peers of similar size and risk, and a terminal growth rate of -10%, -40%, we estimate a value of $12/sh for Arikayce, $18/sh for Brensocatib, $8/sh for TPIP, $0.62/sh for the early pipeline, and $-2/sh for net cash, resulting in $37/sh.

Upside risks: 1) Arikayce full approval, 2) validation of Brensocatib in phase 3, with strong clinical efficacy and no safety concerns, 3) robust efficacy/ safety profile for TPIP in PAH and PH-ILD, 4) growth of translational medicine pipeline, including on-track IND-approvals, and 5) indications of strong commercial support from payers/ community-based providers.

Downside risks: 1) failure to achieve full approval/ commercial expansion of Arikayce in the EU and Japan, 2) failure to meet safety/ efficacy profile in Brensocatib (phase 3), especially due to meaningful infection risk, 3) marginal tolerability improvements, diminished efficacy, and/ or lack of differentiation of TPIP, 4) competition from disease modifying PAH agents, 5) failure of translational medicine pillar, 6) regulatory delays, and 7) commercial pushback from payers/providers.

Kura Oncology (KURA)
Our 12-month price objective (PO) is based on our NPV analysis of revenue forecasts and estimated margin assumptions. We model ziftomenib with the first approval in NPM1m R/R AML in 2025 (LOS 65%), followed by 1L NPM1m in 2028 (LOS 40%), and 1L KMT2Am in 2029 (LOS 30%). We also model tipifarnib in HNSCC with a LOS of 40%. We assume a collective value for the pipeline. Given a WACC of 10%, in line with peers of similar size and risk, and a terminal growth rate between -25% and -50%, based on the timeline, we estimate a value of $31/ share PO, supporting our Buy rating.

Upside Risks to our PO
1) initial approval of ziftomenib in R/R NPM1m AML, 2) by robust efficacy in frontline, 3) favorable efficacy/ safety profile in 1L KMT2Ar AML, 4) durable response in maintenance AML 4) competitive safety and administrative profile, 5) tolerable safety profile of tipifarnib combinations, with no evidence of overlapping TEAEs, and 6) strong commercial support from payers/ community-based providers to broadly administer portfolio candidates.

Downside Risks to our PO
1) failure to achieve approval for ziftomenib in R/R NPM1m AML, 2) poor risk/ benefit of

KMT2Ar AML beyond R/R, especially due to emergence of meaningful DS, 3) lack of clinically meaningful efficacy in frontline and/ or maintenance settings, 4) limited differentiation between ziftomenib and revumenib, 5) DLTs associated with tipifarnib combos, 6) regulatory delays, and 7) commercial pushback from payers and providers.

Analyst Certification

I, Jason Zemansky, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or view expressed in this research report.

US - Biopharmaceuticals Coverage Cluster

Investment rating	Company	BofA Ticker	Bloomberg symbol	Analyst
BUY				
	89bio, Inc	ETNB	ETNB US	Geoff Meacham
	Acumen Pharma	ABOS	ABOS US	Geoff Meacham
	Agios Pharmaceuticals	AGIO	AGIO US	Greg Harrison, CFA
	Amylyx Pharmaceuticals	AMLX	AMLX US	Geoff Meacham
	BioMarin	BMRN	BMRN US	Geoff Meacham
	BioXcel Therapeutics	BTAI	BTAI US	Greg Harrison, CFA
	BridgeBio Pharma	BBIO	BBIO US	Greg Harrison, CFA
	Caribou	CRBU	CRBU US	Geoff Meacham
	CRISPR Therapeutics	CRSP	CRSP US	Geoff Meacham
	Eli Lilly and Company	LLY	LLY US	Geoff Meacham
	Gilead Sciences Inc.	GILD	GILD US	Geoff Meacham
	HUTCHMED	HCM	HCM US	Alec W. Stranahan
	Immatics	IMTX	IMTX US	Alec W. Stranahan
	Insmed Incorporated	INSM	INSM US	Jason Zemansky
	Intellia Therapeutics	NTLA	NTLA US	Greg Harrison, CFA
	Janux Therapeutics	JANX	JANX US	Geoff Meacham
	Keros	KROS	KROS US	Greg Harrison, CFA
	Kiniksa Pharmaceuticals, Ltd.	KNSA	KNSA US	Geoff Meacham
	Krystal Biotech	KRYS	KRYS US	Alec W. Stranahan
	Kura Oncology	KURA	KURA US	Jason Zemansky
	Liquidia Corporation	LQDA	LQDA US	Greg Harrison, CFA
	Lyell Immunopharma	LYEL	LYEL US	Geoff Meacham
	MeiraGTx	MGTX	MGTX US	Alec W. Stranahan
	Merck & Co.	MRK	MRK US	Geoff Meacham
	Mineralys Therapeutics	MLYS	MLYS US	Greg Harrison, CFA
	Neumora Therapeutics	NMRA	NMRA US	Geoff Meacham
	Rani Therapeutics	RANI	RANI US	Geoff Meacham
	Regenxbio, Inc.	RGNX	RGNX US	Alec W. Stranahan
	Revolution Medicines	RVMD	RVMD US	Alec W. Stranahan
	Rocket Pharmaceuticals, Inc.	RCKT	RCKT US	Greg Harrison, CFA
	Royalty Pharma	RPRX	RPRX US	Geoff Meacham
	Sana Biotechnology	SANA	SANA US	Geoff Meacham
	SpringWorks	SWTX	SWTX US	Alec W. Stranahan
	Syndax Pharmaceuticals	SNDX	SNDX US	Jason Zemansky
	Travere Therapeutics Inc	TVTX	TVTX US	Greg Harrison, CFA
	Turnstone Biologics	TSBX	TSBX US	Geoff Meacham
	Vertex Pharmaceuticals Inc.	VRTX	VRTX US	Geoff Meacham
	Werewolf Therapeutics	HOWL	HOWL US	Jason Zemansky
	Xencor	XNCR	XNCR US	Alec W. Stranahan
NEUTRAL				
	AbbVie	ABBV	ABBV US	Geoff Meacham
	Alector, Inc	ALEC	ALEC US	Greg Harrison, CFA
	Amgen Inc.	AMGN	AMGN US	Geoff Meacham
	Arcus Biosciences	RCUS	RCUS US	Jason Zemansky
	Beam Therapeutics	BEAM	BEAM US	Greg Harrison, CFA
	Biogen Inc.	BIIB	BIIB US	Geoff Meacham
	Bristol-Myers Squibb	BMY	BMY US	Geoff Meacham
	Cytokinetics, Incorporated	CYTK	CYTK US	Jason Zemansky
	Editas Medicine	EDIT	EDIT US	Greg Harrison, CFA
	Erasca	ERAS	ERAS US	Alec W. Stranahan
	Esperion	ESPR	ESPR US	Jason Zemansky
	Exscientia	EXAI	EXAI US	Alec W. Stranahan
	IGM Biosciences	IGMS	IGMS US	Greg Harrison, CFA
	Johnson & Johnson	JNJ	JNJ US	Geoff Meacham
	Kymera Therapeutics	KYMR	KYMR US	Geoff Meacham
	Moderna	MRNA	MRNA US	Geoff Meacham
	Pfizer	PFE	PFE US	Geoff Meacham
	Recursion Pharmaceuticals, Inc.	RXRX	RXRX US	Alec W. Stranahan
	Tyra Biosciences	TYRA	TYRA US	Greg Harrison, CFA
	Vir	VIR	VIR US	Geoff Meacham
	Y-mAbs Therapeutics, Inc	YMAB	YMAB US	Alec W. Stranahan
UNDERPERFORM				
	AlloVir, Inc.	ALVR	ALVR US	Jason Zemansky

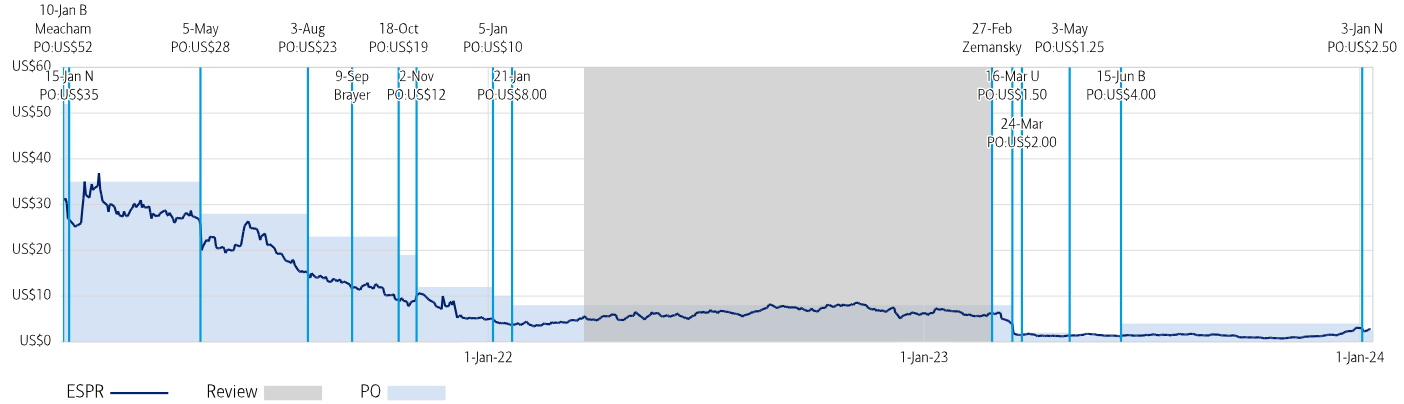
US - Biopharmaceuticals Coverage Cluster

Investment rating	Company	BofA Ticker	Bloomberg symbol	Analyst
	CureVac	CVAC	CVAC US	Geoff Meacham
	Day One Biopharmaceuticals	DAWN	DAWN US	Alec W. Stranahan
	LianBio	LIAN	LIAN US	Geoff Meacham
	Novavax	NVAX	NVAX US	Alec W. Stranahan
	Regeneron Pharmaceuticals Inc.	REGN	REGN US	Geoff Meacham
	Reneo Pharmaceuticals	RPHM	RPHM US	Jason Zemansky
	TG Therapeutics	TGTX	TGTX US	Alec W. Stranahan
	United Therapeutics Corporation	UTHR	UTHR US	Greg Harrison, CFA

Disclosures

Important Disclosures

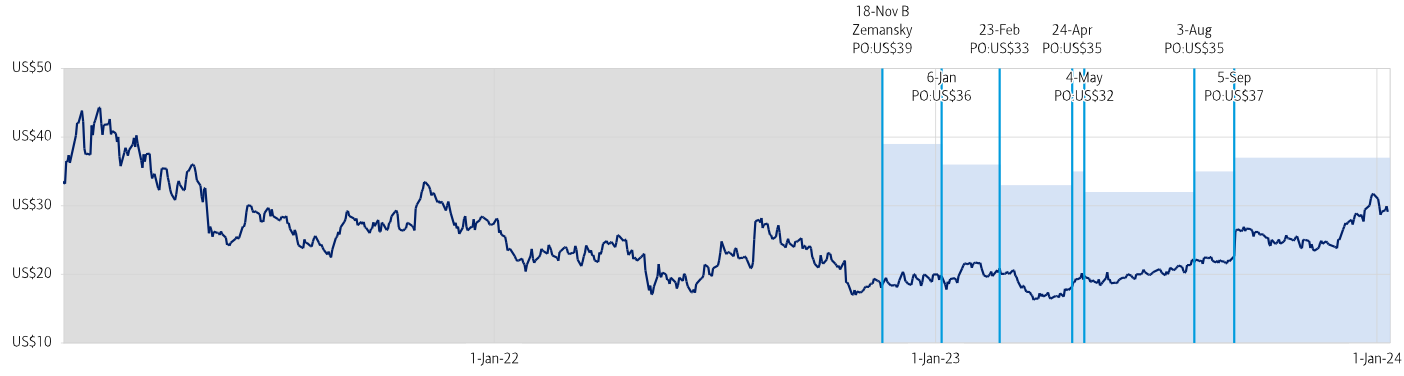
Esperion (ESPR) Price Chart



B: Buy, N: Neutral, U: Underperform, PO: Price Objective, NA: No longer valid, NR: No Rating

The Investment Opinion System is contained at the end of the report under the heading "Fundamental Equity Opinion Key". Dark grey shading indicates the security is restricted with the opinion suspended. Medium grey shading indicates the security is under review with the opinion withdrawn. Light grey shading indicates the security is not covered. Chart is current as of a date no more than one trading day prior to the date of the report.

Insmed (INSM) Price Chart



B: Buy, N: Neutral, U: Underperform, PO: Price Objective, NA: No longer valid, NR: No Rating

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Kura (KURA) Price Chart

B: Buy, N: Neutral, U: Underperform, PO: Price Objective, NA: No longer valid, NR: No Rating

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Equity Investment Rating Distribution: Health Care Group (as of 31 Dec 2023)

Coverage Universe	Count	Percent	Inv. Banking Relationships [R1]	Count	Percent
Buy	234	60.94%	Buy	115	49.15%
Hold	80	20.83%	Hold	36	45.00%
Sell	70	18.23%	Sell	29	41.43%

Equity Investment Rating Distribution: Global Group (as of 31 Dec 2023)

Coverage Universe	Count	Percent	Inv. Banking Relationships [R1]	Count	Percent
Buy	1895	53.62%	Buy	1083	57.15%
Hold	832	23.54%	Hold	454	54.57%
Sell	807	22.84%	Sell	383	47.46%

[R1] Issuers that were investment banking clients of BofA Securities or one of its affiliates within the past 12 months. For purposes of this Investment Rating Distribution, the coverage universe includes only stocks. A stock rated Neutral is included as a Hold, and a stock rated Underperform is included as a Sell.

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Investment rating	Total return expectation (within 12-month period of date of initial rating)	Ratings dispersion guidelines for coverage cluster[R2]
Buy	≥ 10%	≤ 70%
Neutral	≥ 0%	≤ 30%
Underperform	N/A	≥ 20%

[R2] Ratings dispersions may vary from time to time where BofA Global Research believes it better reflects the investment prospects of stocks in a Coverage Cluster.

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