BofA SECURITIES

US Biopharmaceuticals

YA2024: Framing best opportunities within SMID Cap Biopharma

Rating Change

Improving backdrop for SMID Cap Biopharma

Heading into 2024, we are more constructive on our SMID Biotech and Spec Pharma coverage relative to prior years, but the idiosyncratic nature of the space continues to put a premium on stock-picking. At a high level, we remain encouraged by sector fundamentals, including R&D output (contribution to new product approvals) and external demand for biotech innovation (measured by M&A trends). Notably, 2023 was a historically strong year for M&A deal activity (by all measures) offering important external validation for biotech valuation. As we head into 2024, we are further encouraged to see limited FTC M&A pushback and LC biopharma purchasing assets across a wider range of company profiles (by stage + therapy area). Lastly, our analysis (Exhibit 12) suggests a more favorable market environment for companies with high impact catalysts while a tepid '22-'23 biotech IPO market (Exhibit 14) should be aided by decreasing interest rates. Our 2024 top picks are focused on companies with high impact clinical catalysts with a disproportionate risk/reward skew to the upside.

Top picks for 2024: PCVX, TEVA, ITCI, TARS

Our top picks for 2024 are: 1) PCVX which has significantly de-risked its Ph3-ready 24-valent pneumococcal vaccine [VAX-24] with the broadest spectrum of disease coverage. In 2024, PCVX takes aim at full spectrum coverage with its 31-valent product [VAX-31], Ph2 adult data in 2H. In this ~$8bn winner-takes all PCV market we believe the stock is poised for meaningful value step-ups; 2) TEVA – we see the brand/generic hybrid poised for a breakout year keyed by commercial outperformance of key CNS brands and two high impact clinical catalysts (olanzapine LAI + Ph2 TL1A); 3) ITCI – we see the company positioned to continue to deliver solid Caplyta growth in bipolar depression indication with multiple 2024 opportunities to expand the drug's label into adjunctive MDD and mixed features depression; 4) TARS: smaller cap launch story, with Xdemvy for demodex blepharitis quarterly updates serving as key catalysts for attractive new ophthalmology category with blockbuster potential.

Key 2024 sector catalysts

Key 2024 catalysts in our coverage (Exhibit 18): 1) ITCI's Ph3 Caplyta aMDD [1Q/2Q24], 2) IONS: read-across from ALNY's HELIOS-B in 1H24, for TTR-silencer in cardiomyopathy, 3) AXSM's Ph3 Auvelity Alzheimer's agitation [1H24], 4) JAZZ's Ph2b for JZP-385 in essential tremor [1H24], 5) IMVT's '1401 Ph2 data in CIDP [1H24], 6) LYRA Ph3 LYR-210 in CRS [mid-'24], 7) PCVX's Ph2 adult pneumococcal vaccine [2H24]; 8) TEVA Ph3 olanzapine-LAI [2H24], 9) ACLX Ph2 pivotal anito-cel data in RRMM [2H24], 10) TEVA's Ph2 TL1A in IBD [YE24]. Key product launches: BLUE's Lyfgenia for Sickle Cell, TARS' Xdemvy for demodex blepharitis and TEVA's Uzedy (antipsych LAI).

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PO / Rating changes:
ALKS: $29 (prior $27)
ARWR: $37 (prior $29)
GLPG: $44 (prior $41)
HRMY: Neutral to Underperform
IONS: Neutral to Buy, PO $52 to $62
ITCI: $82 (prior $74)
OGN: $11 (prior $12)
PCVX: $80 (prior $67)
PROK: Buy to Neutral, PO $8 to $2
ROIV: $12 (prior $11)
XENE: $56 (prior $52)

Acronyms:
CIDP: chronic inflammatory demyelinating polyneuropathy
CNS: central nervous system
CRS: chronic rhinosinusitis
LAI: long acting injectable
LOE: loss of exclusivity
FTC: federal trade commission
LC: large cap
M&A: mergers & acquisition
(a)MDD: (adjunctive) major depressive disorder
PCV: pneumococcal vaccine
R&D: research & development
RRMM: relapsed/refractory multiple myeloma
IBD: inflammatory bowel disease
TL1A, TTR: drug targets

Tickers: see ticker table on page 9

Contents

Key themes for 2024

Robust M&A adds momentum to biotech into 2024

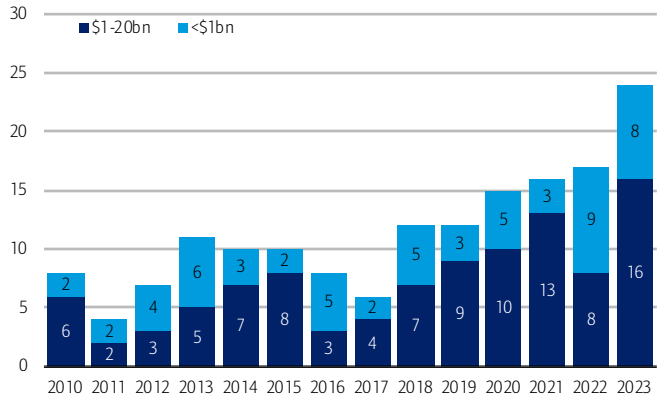
2023 was a record year in biopharma M&A as measured total deal count and overall dollar outlay. In 2023, SMID biopharma showed signs of recovery in 2023 versus 2022 despite underperforming the broader market (XBI: +10% vs. +24%). While 2023 set a high bar for M&A activity, we expect deal trends to persist fueled by solid sector fundamentals (R&D productivity), projected fed rate cuts, and large cap biopharma appetite to fill pipeline gaps.

- **'23 M&A activity came in ahead of historical run-rate**: There were 24 SMID cap takeouts announced in 2023 (defined by $200m-20bn deal size) collectively worth north of $75bn, compared to prior 5-year median of 15 deals totaling ~$42bn in 2018-2022 (Exhibit 1, Exhibit 2). Takeout premiums averaged ~85% which remains consistent with 5-year median level (Exhibit 3). Importantly, about 4 in 5 deals were offered at a premium to the M&A target's stock 52-week high price, a noticeable improvement vs roughly 3 in 5 deals observed in 2020-22 (Exhibit 4).

- **Large cap biopharma's balance sheets remain supportive of potential deal flow**: we measure M&A supply, or 'deal dry powder', by cash and equivalents totaling ~$200bn across 16 LC biopharma analyzed with many having low leverage at below 3x (Exhibit 5). We could caveat that in 2024 some LC biopharma (AbbVie and Bristol Myers Squibb) may focus on smaller sized, bolt-on deals following an M&A splurge (totaling ~$20bn in deals) from each in 4Q23.

- **FTC reviews were not a major issue for SMID size deals but worth monitoring**: FTC (Federal Trade Commission) formed a working group in 2021 to analyze the negative impacts associated with pharma mergers. Since then, we did not observe a major uptick in FTC blocking biopharma M&A especially on SMID size deals (<$20bn). So far, FTC lawsuits have focused on larger-size deals notably Amgen/Horizon and Pfizer/Seagen, though both deals were completed after the acquirers had reached an agreement with the FTC (Exhibit 6). The FTC did not block any SMID biopharma M&A deals in 2022 vs one FTC block on a licensing deal in 2023 (Sanofi/Maze) which seems to be an isolated case (where buyer had a monopoly of the market). With that said, we believe FTC trends merit monitoring given the Maze deal involved a mid-stage asset.

Exhibit 1: SMID Biopharma M&A deal count
2023 was a record year in M&A activity by deal count



Source: Bloomberg. Criteria: deal size of $200m-20bn that involved a publicly traded target.
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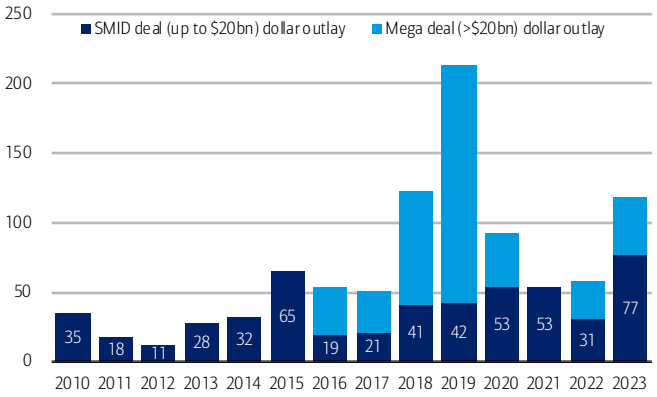
Exhibit 2: SMID Biopharma M&A deal dollar outlay
2023 was also a record year in M&A capital outlay ex-mega deals



Source: Bloomberg. Criteria: deal size of $200m-20bn that involved a publicly traded target.
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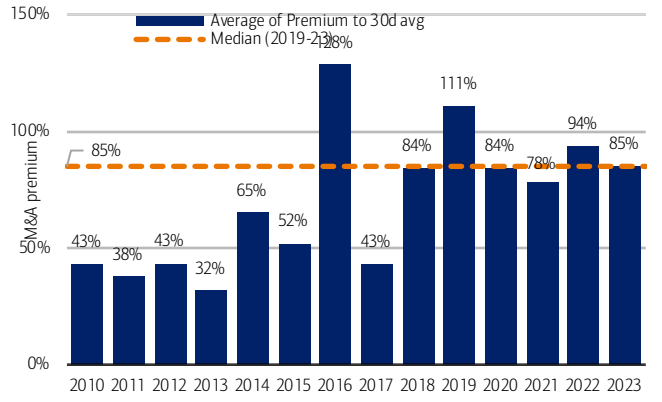
Exhibit 3: SMID Biopharma 30d takeout premium
2023 takeout premiums were consistent with 5-year median



Source: Bloomberg. Criteria: deal size: $200m-20bn, target: public.
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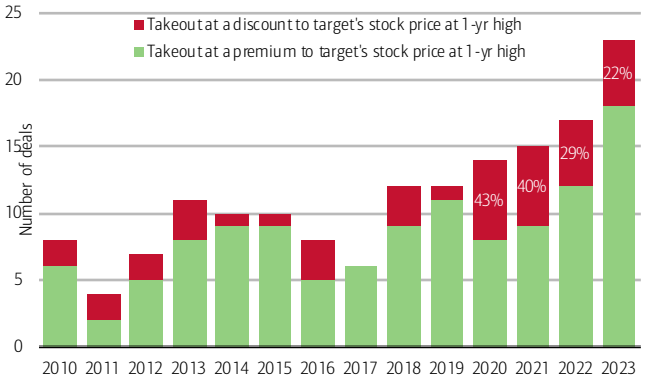
Exhibit 4: M&A offer price vs target's stock price at one-year high
In the last few years, we've seen fewer acquisitions of biotechs below their 1-year share price high point



Source: Bloomberg. Criteria: deal size: $200m-20bn, target: public.
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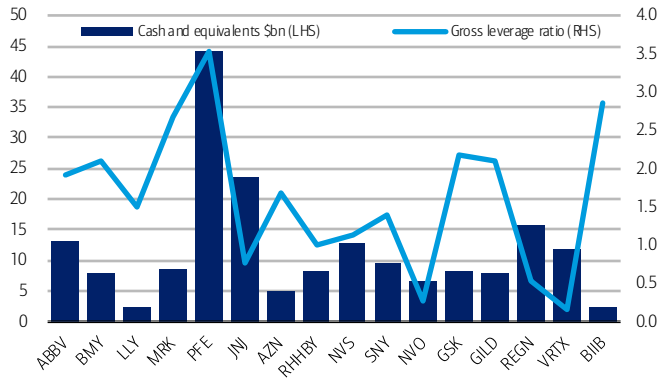
Exhibit 5: LC biopharma's firepower for M&A deals, as measured by cash balance and leverage ratio
Healthy balance sheet from LC biopharma could facilitate M&A deal flow



Source: SEC filings (cash), Bloomberg (leverage, cash). Note: data as of last reporting period (eg 3Q23) thus excludes M&A deals announced in 4Q23 (eg ABBV, BMY).
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Exhibit 6: M&A/licensing deals scrutinized by FTC in 2022-23
There was one licensing deal blocked by FTC in 2023

Deal	Deal announced	Therapy area	Deal size	Outcome	Prohibited conduct
Sanofi-Maze	May 1st, 2023	Rare/orphan	$150m upfront + $600m milestones	Deal terminated	Sanofi terminated proposed acquisition of Maze's Pompe Ph2-ready drug after FTC sued to block the exclusive license. FTC noted the deal would have allowed Sanofi to "maintain its monopoly power" and charge "monopoly prices of over $750,000 for an annual course of treatment for its Pompe therapies"
Pfizer-Seagen	March 13th, 2023	Oncology	$43bn	Deal closed with product donation	To address FTC concerns, Pfizer to irrevocably donate the rights of royalties from sales of Bavencio (avelumab) in the U.S. to the American Association for Cancer Research (AACR). No Seagen products were required to be divested.
Amgen-Horizon	Dec 12th, 2022	&I, rheumatology	$27.8bn	Deal closed with restrictions on product bundling	Amgen prohibited from bundling with newly acquired products. Amgen submits to FTC monitoring of payer contracts related to acquired products and Amgen employees involved in contracting must acknowledge compliance in writing

Source: company reports

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Diversification of LC biopharma M&A offers broader validation for biotech

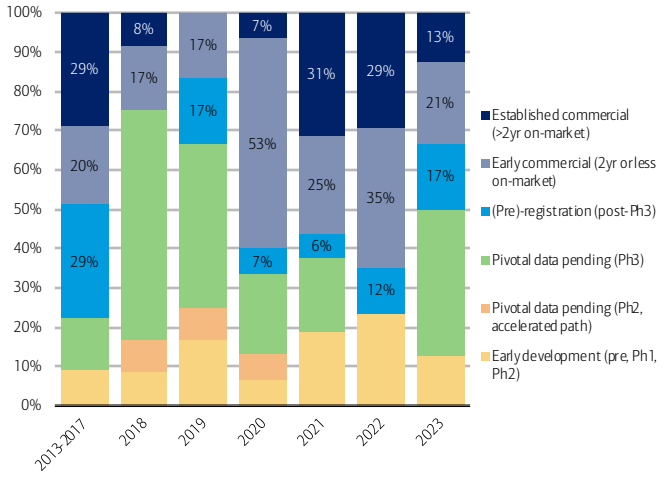
Acquirers more 'agnostic' to asset's development stage: While sector M&A continues to gravitate towards clinically validated assets, we observed half of 2023's takeouts occurred prior to target's Ph3/pivotal data readout vs one-third of M&A in prior 3-year median (2020-22) (Exhibit 7). We note the incremental step-up in 'clinical risk-taking' from acquirers in 2023 could be attributable to: 1) novel mechanism with robust Ph2 data (e.g. anti-inflammatory TL1A), 2) mechanistic validation from competitor pivotal data (e.g. muscarinic), and/or 3) appetite for 'sought-after' drug category (e.g. obesity) and platform technology (e.g. radiopharma).

M&A interest diversifying from historical oncology-centric theme: Oncology historically represented most of the M&A deal flow. While oncology maintained a strong presence in 2023, other therapeutic areas (TA) notably neurology and immunology (I&I) saw increased deal activity (by deal count and/or dollar outlay), with rare disease and cardiometabolic rounding out the top 5 M&A categories in 2023 (Exhibit 9, Exhibit 10). We believe more diverse interest in TA (from large-cap biopharma and investors) bodes well for the sector creating broader validation for a range of therapeutic assets.

Names operating in M&A focus areas outperformed in 2023: similar to therapeutic areas of focus in M&A, oncology, neurology, and I&I names outperformed peers that operate in other TAs in 2023 (Exhibit 8). Oncology outperformance vs other TAs in 2023 could be attributable to recovery from 2021-22 weakness driven by overcrowding in oncology stocks while M&A activity in oncology was at historically low level.

Exhibit 7: M&A by development stage of the target

Preference for post-Ph3/commercial (less risky) assets remains, but acquirers were more willing to take on clinical risks in 2023 vs prior 3 years



Source: Bloomberg, company reports. Criteria: deal: $200m-20bn, target: public.

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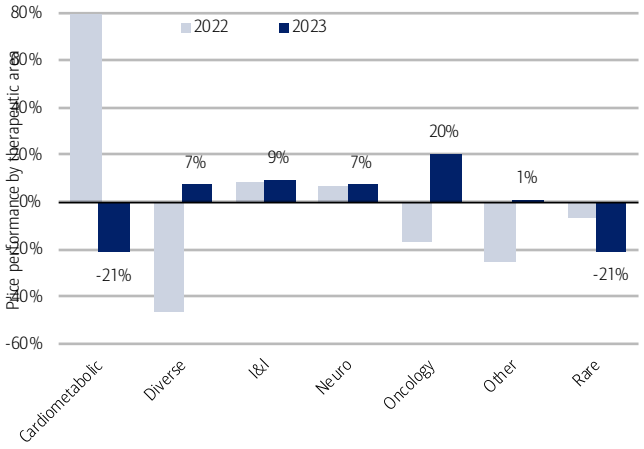
Exhibit 8: Oncology, neuro, and I&I names were among outperformers in '23

Outperformance of onc/neuro/I&I names align with areas of M&A interest



Source: Bloomberg, company reports. Criteria: $1-10bn market cap publicly traded biotech (n=88). Data as of 12/28/23 close.

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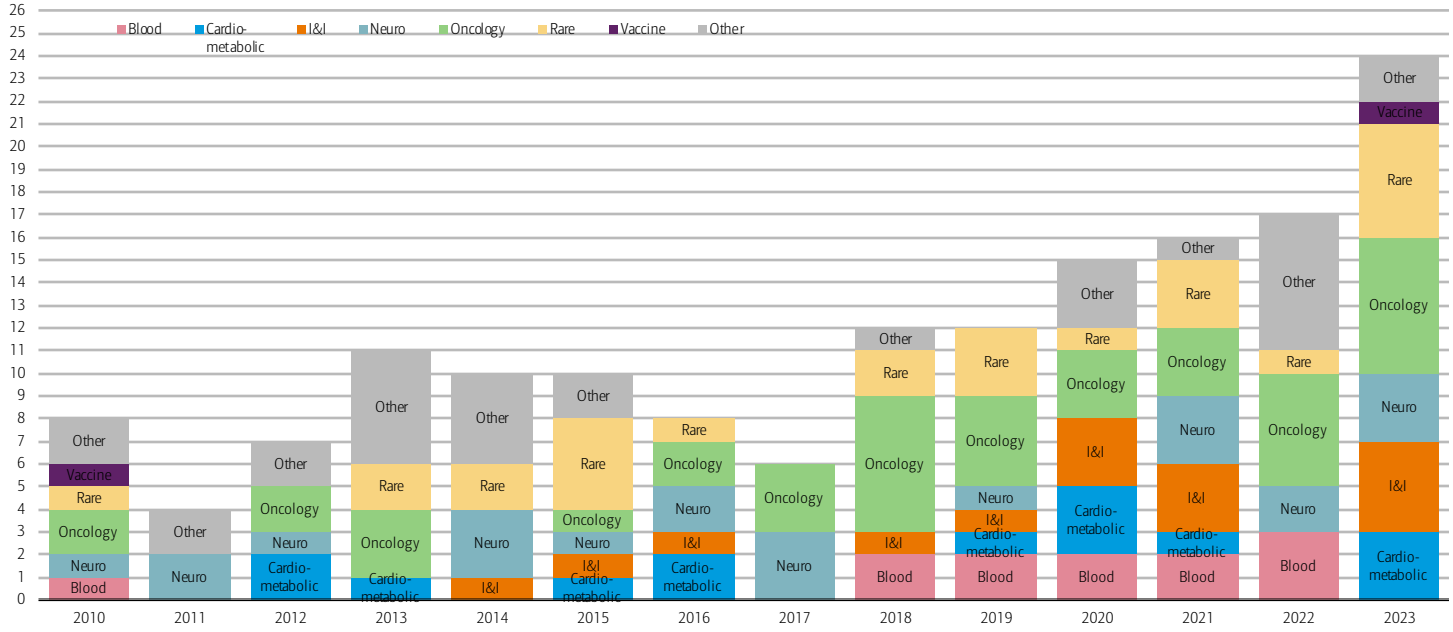
Exhibit 9: SMID Biopharma M&A deal count by therapeutic area (TA)

Most common takeout TAs were cardiometabolic, immunology (I&I), neurology, oncology, and rare disease



Source: Bloomberg, company reports. Criteria: deal size of $200m-20bn that involved a publicly traded target.

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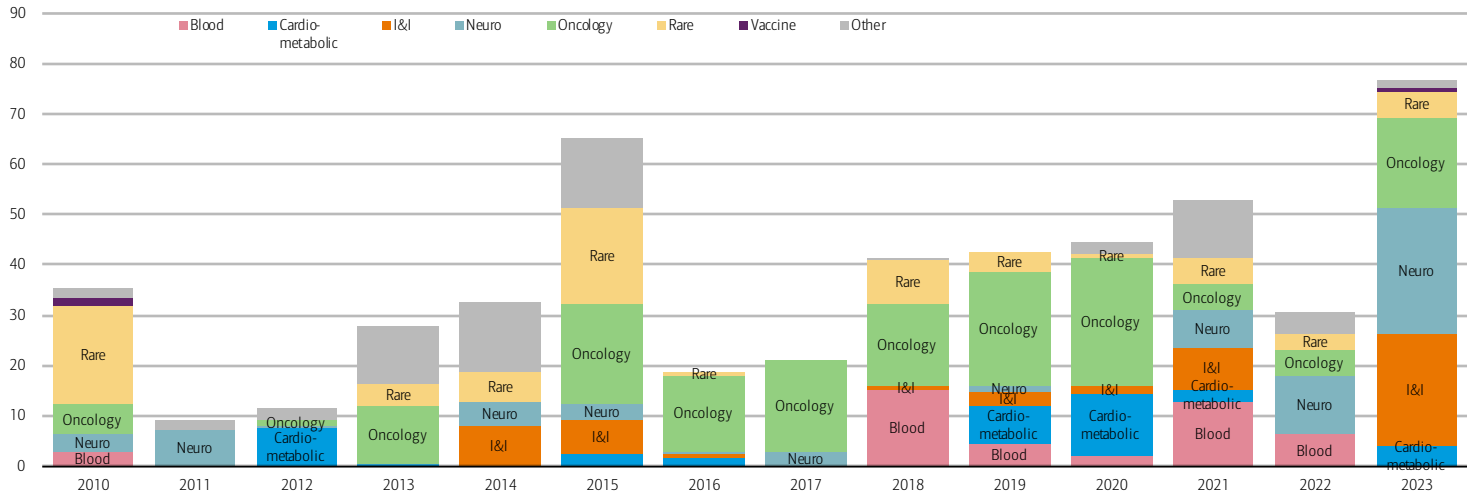
Exhibit 10: SMID Biopharma M&A deal dollar outlay ($bn) by therapeutic area (TA)
Capital outlay was highest among I&I, neuro, and oncology deals in 2023



Source: Bloomberg, company reports. Criteria: deal size of $200m-20bn that involved a publicly traded target.

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Biotech fundamentals remain solid but stock-picking is still at a premium

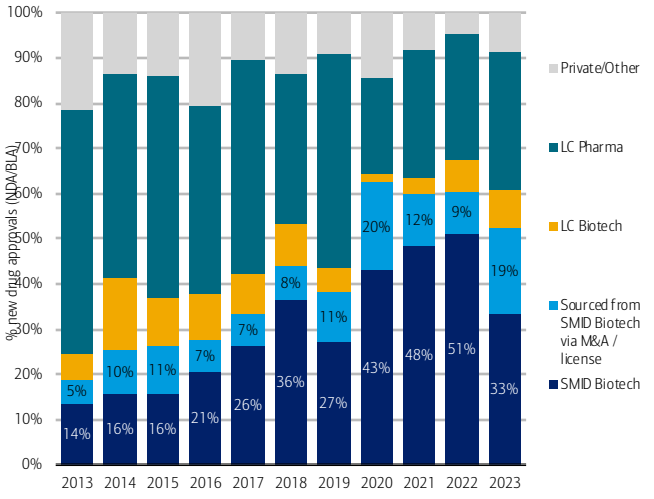
SMID biopharma R&D productivity remains solid: The sector consistently contributed to over half of new drug approvals by the FDA over the past four years (Exhibit 11). This is important as sector M&A activity (as noted) has historically been biased toward clinically validated assets (i.e., registrational or commercial stage).

Catalysts are getting rewarded vs. more challenging 2021 environment: within our coverage, catalyst events proved difficult to navigate in 2021 where we observed modest upside on positive events offset by substantial downside on binary or smaller negatives / inconclusive clinical updates. Encouragingly, catalysts were easier to navigate in 2022 and the trend continued in 2023 (Exhibit 12), as we observed more balanced magnitude of up/down stock moves on positive/negative events.

Nonetheless, sector remains a stock picker space: among 200-300 SMID biotech stocks analyzed with a market cap between $200m and $10bn, 1 out of 4 stocks outperformed broader market (SPX) in 2023 (similar to 2022). That said, we observed a bigger magnitude of outsized positive moves in 2023 vs 2022 (Exhibit 13).

Access to capital in IPO market remained subdued vs prior years: following record number of IPOs in 2020-21, number of new IPOs in 2022-23 remained relatively low at about 11-12 IPO's/year, respectively. Unlike recent years where half or more companies went public at preclinical or early Ph1, the majority of 2023 IPO's were at a more mature stage of development (Phase 2 and higher; Exhibit 14).

Exhibit 11: R&D productivity supports SMID Biotech fundamentals
SMID Biopharma contributed to more than half of new drug approvals by the FDA in 2020-23



Source: FDA.gov (novel NDA/BLA approvals), company reports

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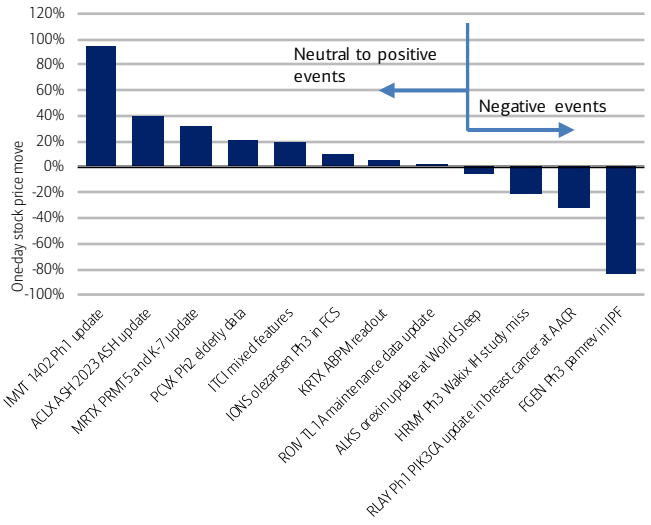
Exhibit 12: Impact of catalyst events on our coverage stock price (2023)
Up/down on positive/negative events were relatively balanced in 2023



Source: Bloomberg, FDA.gov, company reports

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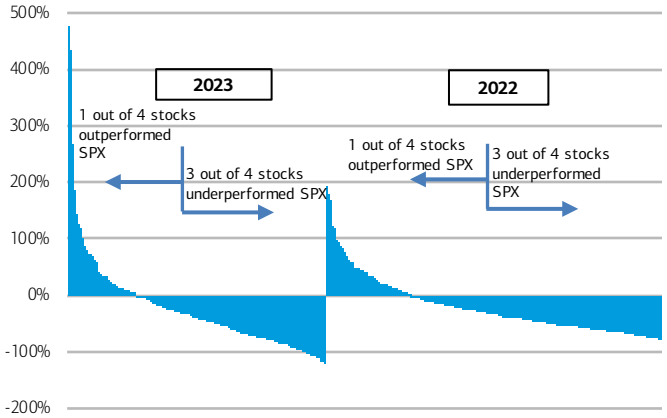
Exhibit 13: SMID Biotech stock price performance vs SPX (2023 vs 2022)
Sector remains a stock picker space, with 1 out of 4 names outperforming SPX



Source: Bloomberg. Criteria: $200m-10bn cap publicly traded Biotech. Note: data as of 12/28/23 close.

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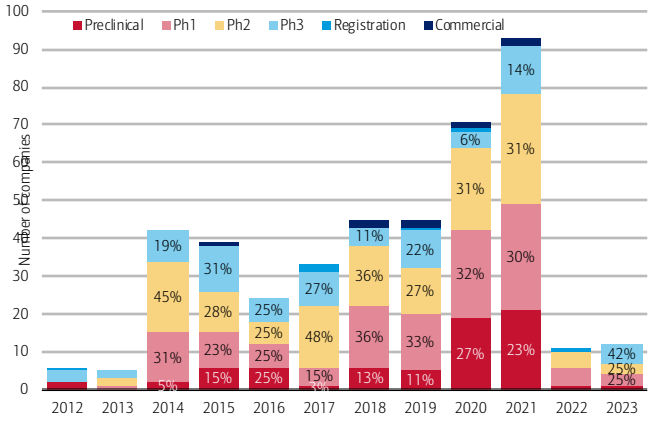
Exhibit 14: SMID biotech IPO by deal count and therapeutic area
2023: deal count remained at historical low level, with majority of companies going public at mid-to-late stage development



Source: Bloomberg, SEC filings. Note: x-axis: deal count, label: proportion (%) of IPOs in a given year.

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Top picks: PCVX, TARS, TEVA, ITCI

Exhibit 15: Summary of top picks
We highlight key focus for our top picks in 2024

Tickers	Company	Stage	PO	Stock price	% vs PO	Key focus, potential catalysts for 2024E
ITCI	Intra Cellular	Commercial	82	72	14%	We see the company positioned to continue to deliver solid Caplyta growth in bipolar depression indication with multiple 2024 opportunities to expand the drug's label into adjunctive MDD and mixed features depression. We also believe '24 should offer added visibility on mid-stage pipeline. Our base case remains Caplyta possessing solid LOE runway until 2033
PCVX	Vaxcyte	Pre-commercial	80	63	27%	PCVX has significantly de-risked its 24-valent pneumococcal vaccine [VAX-24] establishing the broadest spectrum of disease coverage. In 2024, PCVX takes aim at full spectrum coverage with its 31-valent product [VAX-31], Ph2 adult data in 2H. In this ~$8bn winner-takes all PCV market we believe the stock is poised for meaningful value step-ups
TARS	Tarsus	Commercial	42	20	106%	TARS: smaller cap launch story, with Xdemvy for demodex blepharitis quarterly updates serving as key catalysts for attractive new ophthalmology category with blockbuster potential
TEVA	Teva	Commercial	13	10	24%	We see the brand/generic hybrid poised for a breakout year keyed by commercial outperformance of key CNS brands and two high impact clinical catalysts (olanzapine LAI + Ph2 TL1A)

Source: BofA Global Research estimates, Bloomberg

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Summary of model changes

Exhibit 16: Stocks mentioned in this report
Ratings and stock prices of stock tickers mentioned in this report

Ticker	Company name	Rating	Stock price	Ticker	Company name	Rating	Stock price
ACLX	Arcellx Inc	C-1-9	55.76	ITCI	Intra-Cellular Therapies Inc	C-1-9	71.81
ALKS	Alkermes PLC	B-2-9	27.76	JAZZ	Jazz Pharmaceuticals PLC	B-1-9	122.83
AMPH	Amphastar Pharmaceuticals Inc	B-2-9	61.93	LYRA	Lyra Therapeutics Inc	C-1-9	5.18
ARWR	Arrowhead Pharmaceuticals Inc	C-1-9	30.85	OCS	Oculis Holding AG	C-1-9	11.23
AXSM	Axsome Therapeutics Inc	C-2-9	79.61	OGN	Organon & Co	B-3-7	14.43
BHC	Bausch Health Cos Inc	C-3-9	8.08	PCVX	Vaxcyte Inc	C-1-9	63.15
BLUE	Bluebird Bio Inc	C-1-9	1.40	PROK	ProKidney Corp	C-2-9	1.77
EXEL	Exelixis Inc	B-1-9	24.14	RLAY	Relay Therapeutics Inc	C-1-9	11.10
FGEN	FibroGen Inc	C-3-9	0.90	ROIV	Roivant Sciences Ltd	C-2-9	11.20
GLPG	Galapagos NV	B-2-9	40.90	TARS	Tarsus Pharmaceuticals Inc	C-1-9	20.15
HRMY	Harmony Biosciences Holdings I	C-3-9	32.54	TEVA	Teva Pharmaceutical Industries	C-1-9	10.45
IMVT	Immunovant Inc	C-1-9	42.40	VTRS	Viatris Inc	B-3-7	10.85
IONS	Ionis Pharmaceuticals Inc	B-1-9	50.00	XENE	Xenon Pharmaceuticals Inc	C-1-9	46.00

Source: BofA Global research, Bloomberg

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Exhibit 17: Summary of model changes
We summarize rating, PO, and estimate changes made with this report

Ticker	Rating	PO ($)		Revenue ($m)						EPS ($)					
	Change			Old			Current			Old			Current		
		Old	New	2023E	2024E	2025E	2023E	2024E	2025E	2023E	2024E	2025E	2023E	2024E	2025E
ALKS	---	27	29	1,676	1,531	1,540	1,674	1,538	1,550	1.49	2.23	2.24	1.59	2.28	2.28
ARWR	---	29	37	241	0	0	241	0	0	(1.92)	(3.93)	(4.03)	(1.92)	(3.93)	(4.03)
EXEL	---	27	27	1,843	1,980	2,138	1,843	2,029	2,179	0.71	1.26	1.80	0.71	1.25	1.65
GLPG	---	41	44	593	265	268	593	264	267	0.85	(3.65)	(2.90)	0.85	(3.66)	(2.92)
HRMY	Neutral to Underperform	30	30	580	746	912	586	701	817	3.04	4.24	5.43	3.09	3.94	4.86
IONS	Neutral to Buy	52	62	655	610	655	643	618	714	(3.12)	(3.27)	(3.17)	(3.20)	(3.23)	(2.85)
ITCI	---	74	82	469	662	1,218	469	662	1,218	(1.71)	(0.29)	3.80	(1.71)	(0.29)	3.80
OGN	---	11	12	6,242	6,271	6,283	6,242	6,486	6,584	3.78	4.17	4.28	3.78	4.31	4.50
PCVX	---	67	80	0	0	0	0	0	0	(2.85)	(3.15)	(3.14)	(2.85)	(3.15)	(3.14)
PROK	Buy to Neutral	8	2	0	0	0	0	0	0	(0.68)	(0.78)	(0.77)	(0.68)	(0.78)	(0.79)
ROIV	---	11	12	125	157	421	125	157	421	(1.30)	(0.84)	(0.66)	(1.30)	(0.84)	(0.66)
TEVA	---	13	13	15,411	15,623	16,153	15,455	15,879	16,483	2.35	2.44	2.71	2.38	2.48	2.74
XENE	---	52	56	10	5	57	10	5	57	(3.11)	(3.21)	(2.43)	(2.73)	(2.82)	(2.61)

Source: BofA Global Research estimates

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ALKS: We raise our PO from $27 to $29 following inclusion of $92m cash proceeds from sale of a manufacturing facility to Novo and a change in valuation methodology from current DCF to now a blended (50/50) mix of DCF and P/E (13x 2025E). We see P/E as an appropriate valuation metric to include, given increased visibility to ALKS profitability outlook as a pure-play CNS company post-Mural Oncology spin off. Our assumption of 13x '25E EPS is within range of biopharma peers (7-17x) and comparable to 13x where ALKS trades at.

ARWR: We adjust our discount rate to 10% (prior 11%) to align with Ph2/3 companies and increase our pipeline net present value (to $500m from prior $300m) to reflect two new RNAis entering clinic. We now assign ARWR full credit for net cash (vs zero credit prior) to reflect flexibility the company has to limit cash burn in 2024 (i.e. pause initiation of cardiovascular outcome trial) and extend cash runway. These model changes results in new $37 PO (prior $29). We reiterate Buy on our view that Arrowhead offers attractive risk/reward heading into '24 de-risking catalysts.

EXEL: we edge up our Cabometyx (oncology) US forecast by +3% after revisiting '23 volume/price trends. We now forecast $1.77bn (+9%) in Cabo US sales which assumes mid-single digit growth in volume and net price Y/Y in 2024.

GLPG: we raise our PO from $41 to $44 on higher pipeline forecast given early encouraging Ph1 data of GLPG5201.

HRMY: We adjust our Wakix sales forecast to reflect growth through 2028 (LOE assumed in 2029; LOE: loss of exclusivity). In the near term, we expect a slowdown in the pace of patient adds as the launch matures now forecasting 800 patient adds versus prior year's 1.2k adds. We raise our gross margin estimate now more in-line with tiered royalty (entering $600m+ tier in '24) and prior year trends, as well as our R&D estimates in light of next-generation pitsoliant formulation programs.

IONS: We upgrade IONS to Buy (from Neutral), as we see 2024-25 as a catalyst-rich period that can further validate the company's expansive R&D pipeline. We are bullish on four pipeline programs with validating clinical data; each program also represents meaningful commercial opportunity with $300m-$600m peak royalties (high margin) or $600m-$1bn peak sales estimates. Our higher PO of $62 (vs $52 prior) is driven by 1) higher forecast for Wainua on removal of risk adjustment and modestly higher nominal sales on PN approval with a clean label. Given we see positive readthrough to ION' ASO platform, we raise our forecast of IONS' broad pipeline. Net effects to SOTP: +1/shr to Wainua, +2/shr on doni (faster ramp to $600m peak), +$5/shr to broader platform pipeline. We also layer in forecast for ION582 in Angelman based on IONS' preliminary Ph1/2 update in Nov, adding another +2/shr.

ITCI: We add one year to Caplyta's loss of exclusivity (LOE) runway to give credit for its longer dated patents, which results in our new $82 PO (vs $74 prior). We reiterate Buy on our view that Caplyta is positioned to continue to deliver growth in bipolar depression indication with multiple 2024 opportunities to expand the drug's label.

OGN: Our updated forecasts now include Organon's acquisition of Emgality EU commercial rights, modest tweaks to our Nexplanon '24 sales forecast and our revised OpEx estimates reflect SG&A spend presumed for Emgality commercialization.

PCVX: We update our discount rate to 11.5% (from prior 13%) to reflect a blend of Ph2 and Ph3 stage biopharma, which increase our PO to $80 (prior $67). We maintain Buy on our view that PCVX's PCVs offer best-in-class potential on additional de-risking '24+ catalysts.

PROK: We reduce our peak market share for REACT to 0.1%/0.25% in stage 3b and stage 4 market segments (prior 0.4%/0.6%), respectively, to reflect product profile and market unmet need uncertainties with evolving GLP-1 impact on type-2 diabetes CKD market, which decreases our PO to $2 (prior $8). We downgrade PROK from Buy to Neutral on lack of REACT de-risking catalysts (uncertainty on interim analysis) in anticipation of detailed GLP-1 data on eGFR benefit (in 1H24).

ROIV: we increase our PO from $11 to $12 on positive Ph2 data of batoclimab (autoimmune FcRn) in Graves' disease, driven by higher likelihood of success in Graves.

TEVA: We raise our US Gx to reflect stabilization of base generics and cadence of new product launches. Additionally, we raise our Austedo sales forecast expecting $2bn in 2027 vs consensus $2.1bn. The impact of our topline forecast increases on EBITDA are blunted by OpEx increases as TEVA is ramping up S&M spend to support Austedo.

XENE: We update our model to reflect the company's recent equity raise, decrease our discount rate to 10% (prior 11%) to reflect post-recessionary biotech tape and bump our POS for 1101 in MDD to 65% (prior 50%) to reflect Ph2 de-risking data, resulting in new $56 PO (prior $52). We maintain Buy on our view that '1101 is best-in-class seizure asset with blockbuster potential.

Key catalysts for 2024, by company

Exhibit 18: Catalyst tracker for our coverage universe
We highlight potentially impactful catalysts expected in 2024E

Event	Timing (est.)	Ticker and lateral
Ph3 Caplyta adj. MDD	1Q24	ITCI
Ph3 AXS-12 narcolepsy data	1Q24	AXSM
Ph2 TP-05 tick kill study (lyme prevention)	1Q24	TARS
Ph3 HELIOS-B data	1H24 (est Mar/April '24)	Alnylam, IONS
Cabometyx patent ruling	1H24	EXEL
Ph3 Auvelity ADVANCE-2 ADA topline	1H24	AXSM
Ph2b JZP-385 essential tremor data	1H24	JAZZ
Ph3 donidalorsen HAE data	1H24	IONS
Ph2 Period 1 IMVT1401 CIDP data	1H24	IMVT
Ph1 ALKS2680 narcolepsy data update	1H24	ALKS
Ph2 REACT bilateral dosing data, CKD T1/T2D	1H24	PROK
Ph2 TP-04 rosacea data	1H24	TARS
Ph1/2 '582 Angelman's syndrome data	Mid-'24	IONS
Ph3 LYR-210 pre-surg CRS data	Mid-'24	LYRA
Ph2 narcolepsy data TAK861 (orexin)	Mid-'24	Takeda, ALKS
Ph3 ARO-APOC3 FCS data	Mid-'24	ARWR
Ph1 ARO-RAGE high FeNo data	3Q24	ARWR
Ph2 IONIS-FB-LRx GOLDEN trial in geographic atrophy	2H24	IONS
Ph2 VAX-31 adult study readout	2H24	PCVX
Ph3 olanzapine LAI data	2H24	TEVA
Ph1 RLAY2608 + fulvestrant (PI3k) 2L HER2- mBC	2H24	RLAY
Ph3 IMVT1401 MG data	2H24	IMVT
Ph2 pivotal ddBCMA (anito-cel) RRMM data	YE24	ACLX
Ph2 TL1a data	YE24	TEVA
Ph3 Zygel Fragile X data	YE24/early '25	HRMY
Ph3 olezarsen SHTG topline	YE24/early '25	IONS
Ph3 zani GEA data	YE24/early '25	JAZZ
Ph2 OG-6219 endometriosis data	YE24/early '25	OGN

Source: company reports, BofA Global Research estimates

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ACLX: ddBCMA Ph2 pivotal update & BLA de-risking

In 2023, Arcellx (ACLX) outperformed biotech peers (+80% vs +8% XBI) on positive data updates for the company's lead asset, anito-cel (BCMA CAR-T for 5L+ multiple myeloma [MM]) + Gilead partnership updates (milestones and equity investments). Looking to 2024, our focus is on anito-cel Ph2 pivotal data update, (potentially) additional follow-up data from the Ph1/2 study and any other pipeline updates.

- **Anito-cel's Ph1 profile comparable to Carvykti on efficacy; other points of differentiation to be clarified in 2024**: Ph1 update at ASH 2023 supports a anito-cel possessing a competitive profile relative to BCMA CAR-T standard, J&J/Legend's Carvykti on efficacy (durability), whereas potential differentiation: 1) lack of delayed neurotox/parkinsoniasm, so far; 2) better efficacy in pts with extramedullary disease (EMD), and good manufacturing process (Ph1). On efficacy, anito-cel complete response rates and durability of response have been in the same ballpark (est. 28-mo) as Carvykti when adjusting for demographic variables (per MAIC-adjusted Cartitude-1 trial). Post-ASH 2023, we look for clarity on where ddBCMA's mPFS ultimately lands (range: 24-30 months) but we believe efficacy is within the zone of Carvykti. Looking ahead to pivotal Ph2, we look for confirmation (in a larger patient sample) of anito-cel's EMD sub-grp and safety (neurotox) profile.

- **Pivotal Ph2 focus on execution & progression to timely BLA filing**: anito-cel's pivotal Ph2 trial in 5L+ MM (iMMagine-1) continues to enroll, with preliminary data in 2H24E. We view the Ph2 study as de-risked but timely execution is important as ACLX/GILD look to play 'catch up' in the multiple myeloma space. While the exact nature of the 2H24 data update is TBD, we will be focused on complete response rates (mature PFS unlikely) and safety. For CR, reproducing Ph1 CR rate in the mid-70% (76%) would confirm anito-cel's profile (vs 74% from MAIC-adjusted Cartitude-1) ahead of durability data (PFS) given CR correlates with higher PFS. On safety, we will look for anito-cel to show no-worse CRS rate (vs mid single-digit Cartitude-1) and non-existent or very low delayed neurotox/parkinsonism (vs ~5% Caritiude-1). Last, we'd like to see ACLX shorten vein-to-vein time vs. low 20 day in Ph1. Key to our thesis is protracted supply constraints of BCMA CAR-Ts enable anito-cel to catch up despite late-mover status (see report for our CAR-T manufacturing primer).

- **Broader pipeline updates**: first, we will look for initiation of pivotal trial for anito-cel in earlier line MM (iMMagine-2), both on timeline and study population (2L vs 3L MM). iMMagine-2 will be key to expanding anito-cel into the larger market opportunity, e.g. est. 12-21k new US patients per year in 2L/3L MM vs est 4k US incidence in 5L+ (iMMagine-1 population). We will look to competitor updates in 2L/3L MM for read-through: 1) BMY's Abecma – the FDA will host an AdCom to discuss its OS result from the KarMMa-3 trial in 3L+ MM in 2024 (timing TBD). We do not see KarMMa-3 data as a good proxy for anito-cel's efficacy in earlier line MM, considering Abecma efficacy in later lines was well below Carvykti and anito-cel. Of note, Carvykti had an OS benefit with a HR of 0.78 (Cartitude-4 at ASCO 2023), whereas KarMMa-3 did not show OS benefit with OS HR of 1.01 (ASH 2023), 2) Carvykti – FDA action date (2L+ MM) is set for April 5, 2024. An approval here will further validate a role for BCMA CAR-Ts in earlier in MM ahead of ACLX's iMMagine-2 readout. Separately, while early, we look to Ph1 progression and data update (if any) of ACLX-001 in MM. ACLX-001 is ACLX's follow-on BCMA CAR-T asset constructed on the company's ARC-SparX platform.

Acronyms: XBI: S&P Biotech ETF, BCMA: antigen, CAR-T: cell therapy, L: line of therapy, Ph: Phase, MAIC: matching-adjusted indirect comparison, OS: overall survival, HR: hazard ratio, TBD: to be determined, AdCom: advisory committee, ARC-SparX: cell therapy technology.

Exhibit 19: Cross-trial comparison of BCMA CAR-T data
We summarize data benchmark (LEGEND-2) for ddBCMA Ph1 update at ASH 2023

	Abecma	Carvykti				ddBCMA		
	KarMMa	LEGEND-2	CARTITUDE-1	CARTITUDE-1	MAIC adj CARTITUDE-1	ddBCMA Ph1	ddBCMA Ph1	ddBCMA Ph1
	NEJM 2021	J. Hem & Onc 2022	Lancet 2021	ASCO 2022	Curr Med Res Opin 2023	ASH 2022	ASH 2023 abstract	ASH 2023 data
Follow-up (median)	13.3 mo	47.8mo	12.4mo	27.7mo	27.7mo	~15 mo	22mo	26.5mo
Baseline								
n	70 / 54	74	97	97	97	38	38	38
Age	61 / 62	54.5	61	61	62	66	66	66
ECOG								
0	44% / 43%	41%	40%	40%	33%	32%	32%	32%
1	54% / 54%	43%	56%	56%	67%	68%	68%	68%
BMPC ≥60%		---	22%	22%	---	24%	24%	24%
ISS Stage III	17% / 15%	28%	14%	14%	17%	13%	13%	13%
Extra-medullary disease	49% / 30%	30%	13%	13%	~40%**	34%	34%	34%
High risk cytogenetics	29% / 44%	36%	24%	24%	36%	29%	29%	29%
Prior line of therapy	6 / 5	3	6	6	5	4	4	4
Refractory								
Triple	86% / 81%	---	88%	88%	---	100%	100%	100%
Penta	34% / 15%	---	42%	42%	26%	68%	68%	68%
All-comer efficacy								
ORR	69% / 81%	88%	97%	98%	100%	100%	100%	100%

Exhibit 19: Cross-trial comparison of BCMA CAR-T data
We summarize data benchmark (LEGEND-2) for ddBCMA Ph1 update at ASH 2023

	Abecma	Carvykti				ddBCMA		
	KarMMa	LEGEND-2	CARTITUDE-1	CARTITUDE-1	MAIC adj CARTITUDE-1	ddBCMA Ph1	ddBCMA Ph1	ddBCMA Ph1
	NEJM 2021	J. Hem & Onc 2022	Lancet 2021	ASCO 2022	Curr Med Res Opin 2023	ASH 2022	ASH 2023 abstract	ASH 2023 data
CR	29% / 39%	73%	67%	83%	74%	71%	76%	76%
Median time to CR	2.8 mo (1.0-11.8)	---	1.9 mo (1.0-6.5)	2.9 mo (0.9-17.8)	---	---	---	---
6-month PFS	~65% / ~80%	~84%	~87%	~87%	~80%	92%	92%	92%
12-month PFS	~35% / ~35%	~59%	~76%	~76%	~70%	73%	74%	76%
18-month PFS	---	~50%	~55%	~65%	~57%	65%	67%	64%
24-month PFS	---	---	~60%	~60%	~low 50%	---	---	56%
mPFS	10mo / 11mo	18mo	Not reached	Not reached	25.2 mo	Not reached	Not reached	Not reached (K-M est 28mo)
EMD-subgroup efficacy								
ORR	---	82%	---	---	---	100%	100%	100%
CR	---	55%	---	---	---	85%	---	---
6-month PFS	---	---	---	---	---	92%	92%	92%
12-month PFS	---	---	---	---	---	64%	65%	67%
18-month PFS	---	---	---	---	---	64%	65%	67%
24-month PFS	---	---	---	---	---	---	---	~57.5%
mPFS	8mo	8.9mo	---	13.8mo*	---	---	--- ('>18mo)	--- (>24mo)
Safety								
Dose	300m / 450m	0.5m / kg	0.71m / kg	0.71m / kg	0.71m / kg	100m	100m	100m
n	74	74	97	97	---	32	32	32
Grade 3 CRS	10%	10%	4%	5%	---	0%	0%	0
Grade 3 ICANs	0%	0%	9% (neurotox)	12%	---	3%	3%	3%

Source: company reports. Note:*include bone-based and extramedullary plasmacytomas, ** presence of all plasmacytomas, ECOG: status, ISS: International Staging System, EMD: extramedullary disease, ORR: objective response rate, CR: complete response, m PFS: median progression-free survival, CRS: cytokine-release syndrome, ICAN: neurotoxicity, n= subject number, mo: months, ASCO: medical meeting, ASH: medical meeting.

BofA GLOBAL RESEARCH

ALKS: '24 guidance, Lybalvi ramp + Ph1 orexin updates

Alkermes (ALKS) outperformed peers (+14% vs +5% DRG) in 2023. Shares reacted favorably to the company's Vivitrol (addiction) patent settlement and resumption of US Invega (mood disorder) royalty, while an initial negative response to Ph1 ALKS2680 narcolepsy update eventually corrected. In 2023, Lybalvi's (mood disorders) beat-and-raise story didn't materialize and mgmt believes added S&M investment will accelerate utilization in 2024. Heading into 2024, we expect investors to focus on ALKS FY24 guidance (on 4Q call in Feb), clinical updates on orexin drugs (ALKS2680 and competitor Takeda), and Lybalvi performance post-DTC campaign (main investment mid-'23).

- **FY24 guidance marks beginning of profit targets**: in the after-math of shareholder activism, ALKS introduced its value enhancement plan that included out-year profit margin targets starting in 2024-26 (post-spinoff of ALKS' oncology business). Importantly, ALKS has noted oncology operating spend on a trailing basis was around $140-150m (annually; now gone) and $75m of discretionary DTC ad spend for Lybalvi mark key tailwinds necessary to reach ALKS 25% net income guidance (excluding 3% net profit contribution from US Invega royalties). We forecast -14% Y/Y decline in OpEx or -$156m which is slightly higher vs cons ($-143m); see Exhibit 2. for our non-GAAP net income and EBITDA forecast are roughly in-line with ALKS profitability target for 2024.

Exhibit 20: ALKS 2024E forecast: BofA vs cons vs ALKS profitability guidance
Our forecast is in-line with ALKS guidance whereas cons is higher on profitability margins

	BofA	Consensus	ALKS guidance
Revenue	$1.53bn	$1.51bn	TBD
Net income (margin)	$385m (25%)	$375m (25%)	TBD (25%)
EBITDA (margin)	$315m (21%)	$329m (22%)	TBD (20%)
Y/Y % change in OpEx	-14%	-13%	TBD

Source: BofA Global Research, Bloomberg, company reports. Note: TBD - to be determined.

BofA GLOBAL RESEARCH

- **Lybalvi cons calls for +50% '24 growth, aided by DTC**: Lybalvi is on track to generate close to 160k scripts (TRx) in 2023 (vs 145k scripts with 4 weeks of reporting left in Dec), which would translate into est. $56m/$193m net sales in 4Q/FY23. In terms of '24E net sales, we/consensus forecast $294m/$288m which call for +55%/+50% Y/Y sales growth. Assuming low single-digit Y/Y net price tailwind (+3% in '23), cons forecast implies ~+50% Y/Y in TRx script growth (vs ~+100% Y/Y in '23) or roughly +1% w/w TRx growth, which seems achievable if we consider Lybalvi TRx grew +1.2% w/w on average in the past 20 weeks. Swing factors: 1) net price – ALKS expects commercial contracting may negatively impact GTN, 2) volume – additional commercial contracting and DTC campaign (started 2023) may help sustain or boost script trend vs current level.

- **2024 clinical updates key to viability of orexin-class in narcolepsy (NT)**: so far, published clinical data for orexin (OX2R) show the treatment can keep NT patients and sleep-deprived individuals awake at high levels but there remain outstanding questions around safety /tolerability. In 2024, our focus is on Takeda's Ph2 data of its OX2R, TAK-861, which should address the key class safety risk (liver tox; TAK994 stopped due to liver tox), tolerability with longer period dosing and the impact on cataplexy. Also, we look to ALKS' Ph1 data for ALKS2680 in NT2 (and IH) pts to understand utility beyond NT1 and ALKS' Ph2 plan for '2680. For ALKS, we'd like to see more multi-day safety/tolerability data and believe Ph2 doses <10mg daily look the most commercially viable. Both Takeda's TAK-861 and ALKS2680 were designed to be more potent OX2R's aimed at reducing drug dose and improving safety margins though pending Ph2 data for any drug will be needed to get comfortable with liver tox profile. Visual disturbance and cardiovascular tox are other AE's of interest, the former shown in healthy volunteers. See our recent 2024 stretch-event report for a more in-depth discussion of setup for '24 OX2R updates.

Acronyms: DRG – NYSE Arca Pharmaceutical Index, DTC – direct to consumer, NT1/2 – narcolepsy type-1 / type-2, IH: idiopathic hypersomnia, POS: likelihood of success.

AMPH: Baqsimi growth + base biz durability

In 2023, AMPH shares fared remarkably well (+121% vs. +5% DRG), which we attribute to several factors including the acquisition of Eli Lilly's BAQSIMI (glucagon rescue brand; diversification) which has the potential to improve company growth and margins. Also, the company delivered organic growth by capitalizing on a number of drug shortages by ramping up production of in-house generic products. In our view, Amphastar should be able to maintain its peer-group premium multiple if the company can deliver DD bottom-line growth CAGR (BofA/Cons) while we see upside tied to upward estimate revisions (we are more cautious, thus Neutral rated).

- **Baqsimi launch momentum appears strong:** Baqsimi is an intranasally delivered rescue glucagon that differentiates from competition on ease-of-use in emergency situations. Baqsimi is the branded category leader (est. $400m in category revenue) and the drug is growing market share (in growing category). We forecast Baqsimi becoming the most widely used rescue option surpassing generic kits in the next few years and reaching ~$300m in 2030 sales vs. mgmt target ($250-275m peak). We estimate Baqsimi gross margins are around 80% vs. current corporate average of 59%, thus growth of Baqsimi should help expand overall company gross margin by +500 bps longer-term. We see 2024 as a key proof-point in the Baqsimi commercial story as Amphastar has taken over marketing duties and continued momentum of the brand should dispel any concerns around the company's ability to replicate Lilly's marketing of the drug.

- **New products expected but quality of launch candidates is unclear:** AMPH has three new product launch candidates in 2024: g-Forteo and two undisclosed products. Based on recent (4Q23) competitor developments, we see limited opportunity for AMPH to monetize g-Forteo given two competitor approvals plus the launch of an authorized generic for a relatively niche brand (~$600m pre-generic sales). Amphastar has disclosed regulatory action dates on two other new product candidates but the identity of those products has not been revealed yet due to competitive sensitivities. What we know is both undisclosed NP candidates play in Amphastar's core alternative delivery product focus (one metered dose inhaler and one injectable), but it's unclear if these products would be launching into limited competition markets with healthy net pricing.

- **Durability of the base business is also key in 2024:** In the past 3-years, Amphastar has benefited from competitor dislocation in 3 categories: generic rescue glucagon, hospital administered epinephrine and lidocaine. For Gx rescue glucagon, we would not expect prior suppliers of the rescue kits to re-emerge as the category is moving more to branded alternatives. However, both epinephrine and lidocaine have benefited from the supply issues experienced by Pfizer due to the hurricane that hit its Rocky Mount facility, impairing its ability to supply epinephrine pre-filled syringes and lidocaine. On those two products, we would model low-DD and high teens rates of decline (in '24) given risk: 1) Pfizer returning to normal supply - following the restoration of the majority of manufacturing lines at Rocky Mountain with the first shipments of medicines to distribution centers in 4Q23 and full production across the site's 3 manufacturing suites anticipated by the end of 2023; 2) in lidocaine category, Chartwell has emerged as a competitor to monitor.

Acronyms: DD: double digit.

ARWR: Ph1 pulmonary updates are key

In 2023, ARWR was an underperformer (-24% vs +8% XBI) due to cash runway concerns and lack of meaningful (step-up) de-risking catalysts. However, in '23, we believe Arrowhead took key steps to advance its extra-hepatic siRNA platform with ARO-RAGE pulmonary program hitting chronic safety tox and target knockdown milestones. We are buy-rated on ARWR as we believe the company has favorable risk/reward into 2024 that includes catalysts for cardiovascular and respiratory programs with a focus on:

- **'24 data to shape triglyceride-lowering class:** Arrowhead's wholly owned plozasiran (ARO-APOC3) is expected to report Ph3 FCS topline data in 2Q to support an NDA. Furthermore, we expect the company to initiate two pivotal (Shasta) trials in sHTG patients. Competitor IONS' olezarsen will publish detailed FCS data at a 2024 medical meeting which should better inform depth of TG lowering and safety, while Ionis' data for olezarsen in sHTG (late '24/early '25) will better inform the commercial profile of APOC3 category in a large end-market. In '24, we focus: 1) cross-trial comparisons of olezarsen and plozasiran in FCS; and 2) read-across from olezarsen Ph3 in SHTG as a point of validation for the commercial opportunity.

- **Pulmonary franchise (ARO-RAGE) has key clinical readouts in '24** – next year will be important for ARWR's pulmonary franchise with updated Ph1/2 ARO-RAGE data in patients with asthma and high FeNo levels. The benefit of FeNo reduction data is that it would validate ARO-RAGE's ability to drive benefit on the inflammatory biomarker of disease that (hopefully) is similar or better than the 30-40% reduction seen with approved biologics that work downstream of RAGE. Importantly, these data will shape Ph2 dose regimen (dose level and interval) and lead indication prioritization (allergic/eosinophilic asthma or general).

- **Cardiovascular outcomes trial (CVOT) and cash burn flex –** a key overhang on Arrowhead's stock has been cash runway. On the recent F4Q call, mgmt guided to 4Q24 runway and an expected $110m/quarter burn rate which assumes initiation of a large CVOT study towards the 2H24. However, given mgmt is still reviewing whether to advance APOC3 or ANG3 into a CVOT (only 1 not both), it is possible trial initiation could be delayed (modestly extending runway). In 2024, we'd anticipate clarity on Arrowhead's cash funding strategy (partnerships, financings, etc) and we'd note the company has a large asset base which could facilitate a partnership with non-dilutive capital.

Acronyms: ph: phase; NDA: new drug application; FCS: familial chylomicronemia syndrome; sHTG: severe hypertriglyceridemia; TG: triglyceride; FeNo: exhaled nitric oxide; CVOT: cardiovascular outcomes trial

AXSM: Auvelity MDD launch and Ph3 ADA data

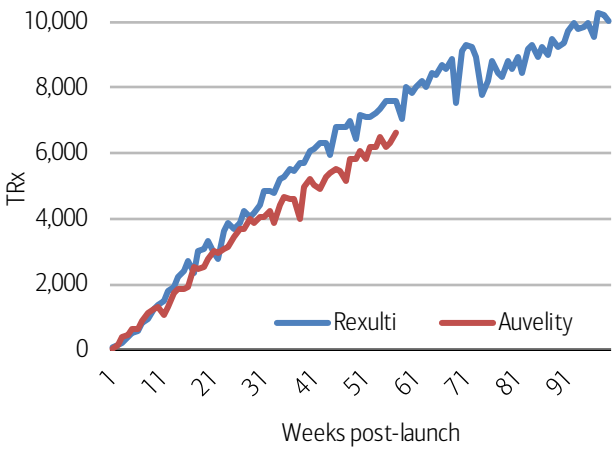
In 2023, AXSM was a modest underperformer (+3% vs +8% XBI) as the Auvelity-MDD launch tracked below consensus, timeline-push for AXS-12 Ph3 narcolepsy and bull case on Auvelity-ADA development path did not materialize. We remain Neutral on AXSM on the view risk/reward is relatively balanced. On the plus side, we expect a couple positive Ph3 readouts (Auvelity-ADA + AXS-12 narcolepsy) counter-balanced by concerns Auvelity-MDD launch tracks below consensus and we have concerns ongoing Auvelity patent litigation caps valuation upside. In 2024, we focus on:

- **Auvelity MDD launch – focus on the impact of expanded salesforce:** in 2023, Axsome did not offer Auvelity sales guidance given net pricing uncertainty (contracting efforts ongoing). In 2024, we'd expect Auvelity reimbursement contracting to improve (vs. 70% covered lives 3Q23) and we'd expect GTN deductions to settle in closer to ~50% steady-state guidance. In 2024, we/cons forecast Auvelity-MDD reaching ~$270m in revenue (+110% Y/Y) which assumes mid/high teens % Q/Q growth vs. +30% average sequential growth in 2H23. If Auvelity-MDD is going to reach cons $1.1bn peak sales, we believe it will be important for scripts to catch-up with Rexulti (comp; Exhibit 21) which reached an estimated $910m in est. '22 MDD sales (Yr-7 post-launch). To that end, Axsome recently announced expansion of the Auvelity sales force (+100 reps) which are expected to have an impact on product adoption in 2H24.

- **Advance-2 topline key to supporting sNDA –** in 1H24, AXSM will report Ph3 (Advance-2) topline data for Auvelity in Alzheimer's agitation. The Advance-2 study data will be needed to establish the long-term safety requirement while it is unclear if the study needs to hit on efficacy to secure approval. The ADA opportunity is a major contributor to our Axsome model, where we assume 80% clinical probability-of-success based on two prior completed Ph3 studies. Our modest POS discount reflects some risk the Ph3 ACCORD trial (small, randomized withdrawal) may not be considered registration-enabling (AXSM has not definitively stated) and general ADA trial risk (relevant to Advance-2). We believe a positive Advance-2 trial would remove a stock overhang while a failed study would cast an overhang on the stock (pending ultimate FDA approval).

- **Numerous potential NDA submissions in 2024:** Axsome will topline data from its pivotal Symphony trial in narcolepsy patients in 1Q24, where it aims to replicate stat sig drug-pbo reduction in cataplexy attacks. We view AXS-12's revenue opportunity in narcolepsy as more niche vs the street (peak sales BofA $355m vs cons $500m) with a relatively undifferentiated profile launching into a (competitively) saturated market. Along with potential AXS-12 narcolepsy NDA (if data are positive), Axsome plans to submit: 1) AXS-14 for fibromyalgia NDA (1Q24) and 2) AXS-07 for migraine (1Q24). We view both NDA submissions as low impact given low value contribution to model (total $7/sh). Axsome plans to submit its Auvelity-ADA sNDA sometime after accruing long-term safety data in 2H24.

Exhibit 21: Launch comparison of Auvelity vs. MDD comparable
Auvelity script volume is trending 15-20% below MDD drug Rexulti at similar timepoints post-launch



Source: BBG; BofA Research

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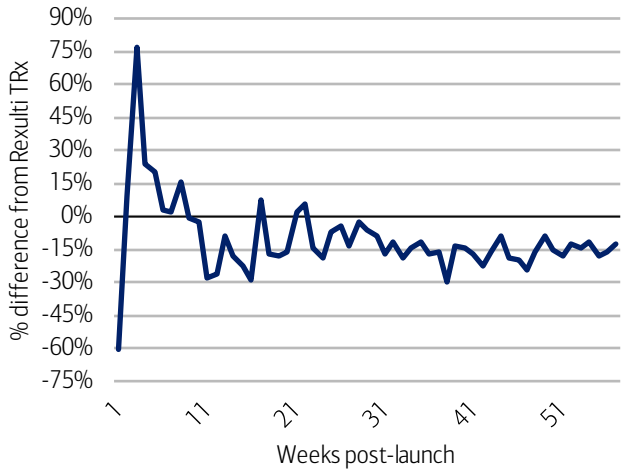
Exhibit 22: % differential in script volumes of Auvelity compared to Rexulti
Auvelity is ~15% lower than Rexulti on a script basis



Source: BBG; BofA Research

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Acronyms: MDD: major depressive disorder; ADA: alzheimer's disease agitation; GTN: gross-to-net; POS: probability of success; Ph: phase; ACCORD, Advance-1/2: clinical trials; (s)NDA: (supplemental) new drug application; stat. sig: statistically significant; pbo: placebo

BHC: Xifaxan IP ruling + implications for eye health spin

In 2023, Bausch Health (BHC) outperformed relative to peers (+29% vs. +5% DRG) due to favorable Xifaxan patent trial updates that included district court rulings upholding an injunction barring the FDA from approving Norwich's generic Xifaxan pending an appeal (decision expected in 1Q24). While the biggest value driver for the BHC stock is the ultimate separation of the eye health business (BLCO), which could result in BHC holders getting BLCO shares worth +66% more than BHC equity, the key question remains timing with the separation process that is now more than 3-years since announcement. Heading into 2024, we believe investors will be acutely focused on the Xifaxan patent appeal as a negative outcome could pose as a barrier to BLCO separation.

- **Xifaxan patent appeal in 1Q24 is key company event**: Bausch expects a Xifaxan patent appeal ruling (Fed Circuit) by 1Q24, after the lower court issued split rulings on the method of use patents and a ruling of non-infringement on 2024-expiring compound patent. We believe the generic challenger will need to secure a favorable ruling on both methods of treatment (IBS and HE) to overcome an injunction put in

place by the lower court. Absent the injunction being removed, it's unclear when /how the Norwich can convert its tentative approval to a final approval. While we believe the NPV of the RemainCo is exceeded by net debt, an earlier than expected generic Xifaxan market entry (vs. assumed 2028 LOE) could significantly pressure RemainCo EBITDA and cash flow.

- **Other factors potentially delaying the eye health spin:** we note a) BHC has yet to hire a CFO, though the company has indicated the interim CFO and accounting team could handle any BLCO equity offerings and/or company separation activities; b) fraudulent conveyance matter – before the US District Court of NJ is a case brought by Bausch investors in common shares and debt seek a declaratory judgment that argues transfer of B&L eye health represents a voidable transfer (e.g. alleges constitutes fraudulent transfer). The Court in this matter denied Bausch's motion to dismiss the lawsuit. Of note, the plaintiffs in the FC case are also pursuing $3bn in damages for securities fraud. We believe this ongoing legal matter represents an important risk factor and could impact any presumed future value transfers in any future company separation.

- **Limited '24 pipeline updates**: BHC recently toplined positive Ph2 data amiselimod (S1P) for ulcerative colitis (UC) though the data were undifferentiated vs four other S1P molecules, while we note the competitive bar is high to both compete and to warrant Ph3 investment. Currently, the market for S1P is dominated by large pharma (BMY and PFE) while there is heavy competitive intensity in UC with other drug classes.

Acronyms: IBS: irritable bowel syndrome, HE: hepatic Encephalopathy, LOE: loss of exclusivity, BLCO: Bausch + Lomb, NJ: New Jersey, FC: Federal Court, S1P: drug target, BMY: Bristol Myers Squibb, PFE: Pfizer.

BLUE: Lygenia Sickle Cell launch (focus on new starts)

In 2023, BLUE shares underperformed (-80% vs +8% XBI) due to cash runway concerns and investor skepticism around gene therapy launches. In 2024, Bluebird will launch its third GT (Lygenia) into the US Sickle Cell market, the largest end-market for its three approved products. Lygenia will face competition from VRTX/CRSP's Casgevy, which is a gene editing approach. In our view, 2024 will be an important year for BLUE to commercially validate Lygenia and address cash runway issues. We remain Buy on BLUE as we see upside to current trading levels on sickle cell disease launch.

- **PRV dispute process low visibility but recent cash raise extends runway** – Bluebird was not granted a rare pediatric priority review voucher (PRV) for Lyfgenia because the FDA determined it failed to meet its requirements (same API approved with Zytenglo). It's unclear to us whether Bluebird will have any success in its bid to overturn the FDA's PRV decision. Following a recent $150m stock offering, we believe BLUE now has cash to potentially bridge the company to profitability.

- **FY24 guidance of 85-105 total patient starts points to momentum of the business** – in 2024, Blue anticipates 85-105 new patient starts across all three of its approved gene products (Lyfgenia for sickle cell, Zynteglo for beta-thal, and Skysona for CALD) which follow process from cell collection to revenue recognition. For Lyfgenia launch preparation, Blue's QTC infrastructure build out is ready for patients to be treated at 35 centers as early as 1Q though we would not be surprised if there was zero 1Q revenue booked for Lyfgenia given vein-to-vein timeline (range 1-3 month). Our FY24 Lyfgenia sales of $55m (vs cons at $76m) assume ~27 treated patients at a one-time upfront cost of $3.1m (gross) per patient. Blue's confidence in setting its $3.1 gross price (higher than Casgevy's price of $2m) is based on positive feedback from payers thus far (100m lives

covered as of year-end '23) where reimbursement agreements are value-based (mgmt is open to negotiations that ensure access to Lyfgenia).

- **Continued execution on Zynteglo and Skysona launch** – we continue to look to commercial performance of Zynteglo (beta thal) and Skysona (CALD) in 2024 to better understand steady-state annual sales contribution. We estimate ~25 patients Zynteglo dosed in 2024 supporting our TDT revenue of $60m (vs cons $63m), and ~10 patients Skysona dosed in 2024 supporting our CALD revenue of $20m. We expect that time to revenue recognition could continue to improve with increased procedural familiarity but might remain slightly varied between patients based on number of cycles needed.

Acronyms: VRTX: Vertex pharmaceuticals (covered by Geoff Meacham), CRSP: Crispr Therapeutics (covered by Geoff Meacham); FDA: food and drug administration; QTC: qualified treatment center; CALD: cerebral adrenoleukodystrophy; TDT: transfusion-dependent beta thalassemia.

EXEL: Cabometyx patent ruling remains key

Exelixis (EXEL) outperformed biotech peers (+50% vs +8% XBI) in 2023, driven by steady Cabo (lead cancer drug; $1.6bn US sales) sales growth, a $500m share buyback and increasing investor appreciation around EXEL's broad patent estate (to drive favorable IP resolution). In 2024, we are focused on continued Cabo sales growth, Cabo patent resolution (settlement or court ruling), and pipeline updates -- focus is on zanza (son-of-Cabo) and XB002 (tissue factor [TF]- ADC).

- **Cabo exclusivity runway**: In a second bench trial (see report) concluded Oct 26th 2023, a second set of Cabometyx patents were litigated: (1) malate salt patents ('439/'440/'015) expiring in Jan 2030; and (2) formulation patent ('349) expiring in Feb 2032. Absent a settlement, we would expect a ruling for the case around 1H24 based on the historical analogs (no earlier than Feb. 20 post-trial briefs). We believe the further the legal matters goes without a settlement, there is a risk the Street starts to discount more negative outcomes (given investor aversion to predicting patent trial outcomes). We believe there are three possible trial outcomes: (1) EXEL loses on malate salt ('439/'440/'015) and formulation ('349) patents – this is worst case and we'd assume MSN's generic could enter the market September 2026 (possibly early '27 if pediatric extension granted), pending any appeals and assuming MSN could secure FDA approval of its generic product (TBD); (2) EXEL prevails on the malate salt patents but not the formulation patent – Jan 2030 LOE for Cabo; and (3) EXEL prevails on the formulation patent – Teva can enter in 2031 (per settlement) while MSN would be blocked to 2032. See Exhibit 23 for our DCF up/down estimates on LOE outcome scenarios.

Exhibit 23: Scenario DCF analysis of EXEL
We estimate DCF valuation on an ex-pipeline bases, based on timing of Cabo generic entry

LOE assumption	DCF	DCF (ex-pipeline)
August 2026	18	16
January 2029	25	22
January 2030	27	24
January 2031	29	26

Source: BofA Global Research estimates. Note: DCF only includes our forecast of Cabo in approved indications.

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- **FY24 guidance**: we expect EXEL to provide FY24 guidance in early January (same as prior practice). On guidance, our focus is on topline and product sales guidance (majority driven by Cabo US sales) and OpEx. Cabo volume growth in 2023 was driven by a combination of higher market share and longer duration of therapy

(DOT). We will look to management commentary on Cabo growth drivers vs +9% Y/Y script growth in 2023, while DOT may start to approach steady state. We/cons forecast $1.77/$1.85bn in Cabo US sales (+9%/+14%). Our forecast assumes around mid-single digit Y/Y growth in volume and net price (vs 4-5% net last year), whereas cons forecast is more bullish implying continuation of +9% Y/Y TRx growth. On OpEx, we will look to EXEL's plan for R&D expenditure as the pipeline portfolio continues to progress with Zanza and XB002 in mid-to-late stage clinical trials. We and cons forecast $1.03bn and $10.9bn in 2024E R&D spend, respectively, relative to $1.05-1.075bn range for FY23.

- **Pipeline updates could be limited in '24E**: in 2024, the only late-stage pipeline update will be detailed data presentation of CONTACT-02 (cabo/atezo in prostate cancer) in early 2024 (we note ASCO GU as a possible venue). For CONTACT-02, we believe OS benefit will be needed for commercial success and possibly regulatory approval, though EXEL has not confirmed whether early 2024 data will include any interim OS data. Recall, CONTACT-02 hit primary PFS endpoint and showed a trend toward improvement of OS (though not statistically significant), with the trial continuing to OS analysis (timing not specified). A key prostate competitor is Novartis Pluvicto which had data (from PSMAfore trial) presented at ESMO 2023. On the broader pipeline, our focus is on: 1) zanza – the next-gen Cabo is being studied in 3 pivotal trials (CRC, nccRCC, head and neck) and Ph1/2 dose expansion cohorts (additional tumor settings). We will look for any new Ph1/2 data and/or Ph3 trial initiations; 2) XB002 – monotherapy is in dose expansion and dose escalation work is ongoing for combination strategies. EXEL's commentary at recent R&D Day (Dec) suggest possible data update in 2024.

Acronyms: MSN: MSN Lab, FDA: US Food and Drug administration, LOE: loss of exclusivity, TBD: to be determined, TRx: script, OS: overall survival, PFS: progression free survival, CRC: colorectal cancer, nccRCC: non-clear cell renal cancer, ASCO GU, ESMO: medical meetings.

FGEN: pivot to oncology with pamrev Ph3 + FOR46 Ph1 readouts

In 2023, FGEN shares underperformed (-94% vs +8% XBI) on the failure of Ph3 pamrevlumab trials in IPF and DMD. In our view, 2024 outlines a difficult catalyst path with high risk Ph3 pamrev readouts in 1H24 and preliminary data from cancer asset, FOR46. In 2024 we focus on:

- **Pamrev's pancreatic cancer topline data** – in 1H24, pamrev has two readouts in pancreatic cancer – 1) ph3 LAPIS trial in locally advanced unresectable pancreatic cancer patients (1Q24) and 2) Ph2/3 trial in metastatic pancreatic cancer (1H24). The rationale for pamrev in pancreatic cancer comes from preclinical evidence of improvement of survival in mouse model of pancreatic cancer and Ph1/2 trial where treatment with pamrev did not elicit a higher ORR than the average chemotherapy response rate (~low-to-mid teens). Topline data from LAPIS trial will assess pamrev's overall survival (OS) when added to standard chemotherapy, where a stat sig improvement is necessary for approval. We view both readouts as low probability because pancreatic cancer is very difficult to treat and pamrev has loose scientific rationale and assign 0 value to pamrev in our model.

- **FOR46's (FG-3246) two Ph1s (mono + combo) data in mCRPC** – management hopes to pivot focus to its oncology pipeline as its next leg of growth and is advancing FOR46, an antibody drug conjugate (with chemotherapy payload) against CD46 receptor present on cancer cells, in Ph1 trials. Ph1 trials are assessing FOR46 in mCRPC where monotherapy trial will dose escalate and assess safety expansion (1Q24 topline) and combo trial will assess FOR46 in combination with enzalutamide

(2H24 topline). Focus for the topline data will be on ORR and safety profile that are consistent with approved ADCs. We currently exclude FOR46 from our model given high risk and look for Ph1 data to offer some validation on clinical activity in the difficult to treat mCRPC population.

- **Clarity on Roxa-China patent rulings** – though it is unclear whether Fibrogen will be in a position to offer an update on Roxa's China patent challenges in 2024, we await any future clarity on patent rulings pertaining to Roxadustat's crystalline patents. Roxa for the treatment of anemia in CKD is the main value revenue driver for FGEN. Its near-term revenues are at risk given uncertainties on generic entry which depend upon court decision on appeal reversal. Roxa's crystalline patents expire in 2033 but if prior unfavorable rulings are upheld, generic entry could occur as early as 2025. We model an LOE in 2026 and await any updates on ruling process from management.

Acronyms: IPF: idiopathic pulmonary fibrosis; DMD: Duchenne muscular dystrophy; ORR: overall response rate; mCRPR: metastatic castration-resistant prostate cancer; CD46: receptor on cancer cells; ADC: antibody conjugates; CKD: chronic kidney disease; LOE: loss of exclusivity.

GLPG: progression of CD19 CAR-T and pipeline expansion

In 2023, Galapagos (GLPG) underperformed relative to biotech peers in 2023 (-8% vs +8% XBI) as the commercial launch of Jyseleca EU was negatively impacted by a JAK-class label (EU) update, coupled with a lack of meaningful pipeline updates that could drive value inflection for the stock. With GLPG divesting Jyseleca EU commercial rights, we expect investors to focus on the progression of GLPG's lead CAR-T program into a pivotal trial while further validating GLPG's point-of-care manufacturing model, as well as GLPG's business development plans to bolster its pipeline portfolio.

- **Initial data of CD19 CAR-T in CLL encouraging; IND in 2024**: Ph1 update of GLPG5201 (CD19 CAR-T) presented at ASH 2023 in r/r CLL and RT (Richter transformation; complication from CLL) was encouraging. The Ph1 update featured 14 pts, of which 8 received proposed RP2D. ORR/CR rates were 93%/57% across all dose levels and 100%/63% at RP2D, which look better on response rates relative to 3L+ competitor Lilly's Jaypirca (72% ORR, no CR) although sample size was small and duration of follow-up is limited to draw any conclusion on durability of efficacy (PFS) at median follow-up of 6 months. As of the data cutoff, 77% still had ongoing responses. In 2024, our focus is on 1) data update for GLPG5201 in a larger sample size and longer follow-up, 2) IND clearance for GLPG5201 and activation of US trial sites and additional EU trial sites, with a focus on mfg success rate, level of automation (eg how many operators required at a time for 50 product runs), and reproducibility of mfg process at a larger scale (vs a handful of EU sites currently). Initial Ph1 data indicate there is room to improve for '5201 mfg process, given 3 out of 12 pts (25%) received a lower dose level than RP2D due to lower mfg CAR+ T-cell yield, which would have been considered a relatively high out-of-spec rate among approved CAR-T therapies in real world. Vein-to-vein time was 7-days (median) vs. range of 7-14 days vs GLPG's aspirational goal of 7-day vein-to-vein time. GLPG also presented data of GLPG5101 (CD19 CAR-T) in r/r NHL, though differentiation vs established CD19 CAR-Ts is TBD and we note the CD19 segment does not face supply constraints observed in the BCMA segment.

- **BCMA CAR-T advancing through Ph1**: persistent BCMA CART supply constraints and the large multiple myeloma market (est. $8bn) offer room for multiple CAR-T players to compete. Conversely, GLPG is in early Ph1 and several years behind multiple BCMA CAR-T players (Bristol's Abecma, Legend's Carvykti, Arcellx's anito-cel, Gracell's GC012F) thus it is TBD whether GLPG can catch up / capture

meaningful market share. GLPG dosed first Ph1 patient in Dec'23. Timing for initial Ph1 data update is TBD (likely late 2024 or 2025 event), we will look for management's commentary on Ph1 dose escalation experience and comparability of point-of-care delivery and manufacturing success rate vs experience with its CD19 CAR-T programs. Gilead can opt into GLPG's program post-Ph2 but is investing significantly in its partnered (Arcellx) centralized autologous BCMA CAR-T.

- **Business development to bolster pipeline**: while GLPG has signaled its intention to conduct business development (BD) to bolster its R&D pipeline, the company has not in-licensed or acquired additional pipeline assets since the acquisition of CellPoint and AboundBio in 2022. While GLPG's CAR-T programs carry an interesting value proposition of point-of-care delivery, we would argue the company's current immunology pipeline is targeting crowded or niche indications with unclear point of differentiation, e.g. GLPG3667 (TYK2 inhibitor) for lupus and dermatomyositis. GLPG remains committed to oncology and immunology as key therapy areas. On its 3Q call, GLPG noted the company was "actively pursuing multiple deals" in those two TA's and framed its approach as "highly selective".

Acronyms: CD19, BCMA: antigens, CAR-T: cell therapy, JAK, TYK2: drug targets, CAR+ T-cell: modified T cells, pts: patients, mfg: manufacturing, TBD: to be determined, IND: investigational new drug, ASH: medical meeting, RP2D: recommended Ph2 dose, ORR: objective response rate, CR: complete response, PFS: progression free survival, CLL chronic lymphocytic leukemia, RT: Richter transformation, NHL: non-Hodgkin's Lymphoma, r/r: relapsed/refractory, TA: therapeutic areas.

HRMY: Wakix growth + pipeline data updates

In 2023, HRMY underperformed (-41% vs +5% DRG) relative to the pharma index with weakness attributable to: 1) a short-seller report which was issued in conjunction with an FDA Citizen's Petition seeking to get Wakix removed from the market – resolution remains TBD though we believe it is unlikely the product gets pulled; and 2) Wakix Ph3 IH study missing its primary efficacy endpoint. In 2024, we expect investor focus to remain on 1) Wakix commercial performance in approved narcolepsy indication, 2) Zygel Ph3 data readout for treatment of Fragile X syndrome – possibly by late 2024, and 3) next-generation pitolisant clinical data updates which could provide some visibility around pipeline products that could generate revenue beyond the Wakix LOE.

- **Wakix performance remains central to stock performance:** In 2024, Harmony enters year 5 in the launch of Wakix (pitolisant) as a treatment for narcolepsy. We expect Wakix to reach $580 in 2023 sales (+33% Y/Y) based on 11% market share of the addressable US market. While there has been increased competition in the category (new oxybate alternatives), Wakix has appeared relatively insulated from oxybate competitive dynamics with (per mgmt) no changes in payer formulary coverage. As we think about 2024 patient adds, we note Wakix adds on a yearly basis should start to decline given the maturity of the launch and challenge of growing versus more challenging (larger) prior year comps. In the absence of indication expansion (we don't expect the FDA to approve IH based on existing data), we forecast $701m in 2024 sales below cons $713m (0.8k adds vs. 1.2k prior year) + modest Y/Y net price appreciation.

- **Pivotal Fragile X represents a data wildcard:** In 2024, Harmony could potentially readout Ph3 results for Zygel (topical cannabidiol) as a treatment for Fragile X Syndrome. The Zygel asset came to Harmony through an $60m upfront acquisition with an additional $30m milestone if the program gets to positive Ph3 data readout by end of 2024 vs. $20m milestone if positive readout occurs by June 30, 2025 ($10m milestone thereafter). In a prior Ph2, Zygel failed to reach stat sig efficacy on its primary efficacy endpoint (ABC-C FXS / Aberrant Behavior Checklist-Community

Fragile X Factor Structure) but Harmony was encouraged by post-hoc data in patients with complete methylation (60% of 80k US patients with Fragile X) that it was willing to further invest in the program. The ongoing Ph3 thus differs in the evaluable patient population and more narrower enrollment criteria could be a factor in pace of enrollment. Ultimately, the Zygel Ph2 data are the only randomized, controlled data evaluating cannabidiol (any form) for treatment of FXS, which likely explains why Zynerba traded at <$20m market cap prior to the acquisition and Harmony was able to get the asset for a low upfront.

- **Next-gen pitolisant vs. Wakix patent litigation updates**: On 8/14, Harmony received its first Wakix Paragraph 4 certification which has patents expiring 2026-30. No trial date has been scheduled, but in our experience trials tend to occur >2-years of litigation (discovery), thus we would not expect any actionable updates around P4 litigation (though settlements can occur at any time). Broadly speaking, the risk for a single product company with a patent litigation event is the risk that a perceived overhang limits investor appetite to own the stock. To that end, Harmony is looking to advance its next-generation pitolisant programs through clinical development with updates in 2024. The Harmony LCM (lifecycle management) strategy includes: 1) Formulation 1: enhanced formulation designed to deliver an optimized PK (pharmacokinetic) profile and a higher dosage strength, as well as extend IP runway 2040+; and 2) Formulation 2: modified formulation with potential clinical differentiation with an opportunity to launch within the Wakix lifecycle. For the more abbreviated Formulation 2, we see limited room for upside from formulation-tweaks, while we believe Ph2 proof-of-concept data will be needed for the more novel Formulation 1 before investors can assign meaningful value.

Acronyms: LOE: loss of exclusivity, IH: idiopathic hypersomnia, IP: patent

IMVT: Ph2 CIDP + Ph3 MG studies key proof-points on FcRn differentiation

In 2023, IMVT shares outperformed (+140% vs +8% XBI) driven by positive clinical updates for IMVT1402, the companies follow-on FcRn antibody. The emerging profile of '1402 suggests the drug could be differentiated on dosing (the only simple SQ) and potentially on efficacy (TBD). In 2024, we look to two clinical readouts to help confirm whether deeper IgG reduction achieved with IMVT's higher dose strength translates to added clinical benefit with a bigger focus on the Ph2 CIDP trial. Otherwise, 2024 is largely going to be about broader execution of the '1402 clinical program that will be informed by FDA meetings (1H24 IND clearance). In 2024, we focus on:

- **Bato Period 1 CIDP data 1H24 to inform dose-response** – a key catalyst in 2024 will be Ph2b bato (first-gen FcRn) data from a CIDP trial which is designed in two parts: period 1, open label randomized treatment phase (data 1H24) and period 2, randomized withdrawal phase. Batoclimab is assessing two doses – low dose: 340mg (65% IgG reduction) and high dose: 680mg (75% IgG reduction) in period 1 to determine whether higher dose will drive higher responder rate. The outcome of Period 1 will determine asset prioritization where a clear dose-response would support advancing '1402 for CIDP. We view >10% delta between high and low dose as meaningful and believe investors will be looking to compare low dose to Vyvgart's 67% (Stage A).
- **1402 disease prioritization (CIDP, RA, MG)** – Immunovant plans to submit an IND for 1402 to the FDA by 1H24. After IND clearance and CIDP trial read out (Period 1 in 1H24), Immunovant will be in a position to outline '1402 indication prioritization, which could include CIDP, MG, and RA. Deeper IgG reductions could be important in driving better clinical benefit in highly inflammatory diseases where processes beyond single auto-antibody are

driving disease pathophysiology, such as RA and CIDP. 2024 competitor data from efgartigimod in PV (pemphigus vulgaris) could offer some read-through to the breadth of FcRn opportunities while a recent competitor failure (efgar in ITP) appears to be lower on IMVT's priority list (small market).

- **Ph3 MG topline + other catalysts –** batoclimab is anticipated to read out topline data from Ph3 MG trial (registrational enabling) in 2H24, which would lead to an NDA, if positive. Here, we look for data similar to prior Ph2 data where the high dose (680mg) drove higher number of super responders (pbo-adj. change in MG-ADL > 4-5 points).

Acronyms: CIDP: chronic inflammatory demyelinating polyneuropathy; IgG; immunoglobulin antibody; MG: myasthenia gravis; RA: rheumatoid arthritis; NDA: new drug application; PV: pemphigus vulgaris; ITP: immune thrombocytopenic purpura; MG-ADL: myasthenia-gravis activities of daily living scale.

IONS: competitor HELIOS-B + several IONS pipe updates

In 2023, Ionis (IONS) outperformed biotech peers (+32% vs +8% XBI) on pipeline progress updates (e.g. positive olezarsen Ph3 readout in FCS) and (potentially) anticipation of a busy 2024 catalyst calendar. In 2024, we are most focused on:

- **Eplontersen PN launch and competitor ALNY's CM Ph3 readout (HELIOS B)**: IONS' eplontersen (partnered with AstraZeneca) is about 1-year behind ALNY's vutrisiran and requires more frequent dosing (SQ-monthly vs. SQ-quarterly). IONS Ph3 CM trial will readout in 1H25 at the earliest, though we/investors look to read-across from ALNY's HELIOS B study, including results in primary composite endpoint, key secondary endpoints (eg mortality, hospitalization), and subgroup analyses (eg tafamidis use). Broadly speaking, we view validation of TTR silencers' efficacy in CM and differentiated benefit vs standard of care tafamidis as key to IONS upside. Conversely, modest benefits from TTR silencers and lack of differentiation vs. tafamidis could reduce investor enthusiasm for eplontersen and/or the silencer class in CM. IONS' Ph3 is ~2x larger than HELIOS B (Exhibit 24) thus better powered to detect benefits in or subgroup analyses, though whether IONS' more conservative Ph3 powering assumption will translate to a more competitive label is TBD. See our 2024 stretch-event report for a more detailed write-up of HELIO B read-through to IONS, and see report for takeaways from our recent Bus Tour meeting where IONS framed potential path to a win in CM. Separately in PN, we will track eplontersen launch sales vs ALNY's vutrisiran and patisiran. ALYN's vutri- and patisiran collectively generated annualized net sales of ~$540m in the US and ~$920m WW as of 3Q23. IONS plans to primarily focus on identifying new patient starts for eplontersen launch citing <20% treatment rate.

- **Mid-year Ph1/2 data of ION582 in Angelman syndrome**: with the Ph1/2 study (HALOS) fully enrolled, management plans to provide a mid-'24 study update that includes: 1) full Part 1 or MAD data (4-mo treatment) and a cut of the Part 2 LTE (12-month but duration will possibly be extended) which is expected to inform end-of-Ph2 FDA meeting while best case Ph3 start time is 2025. Management has refrained from articulating any specific efficacy bars for Ph1/2 success (TBD given lack of defined registrational endpoint), offering loosely defined "significant" benefit. Biogen can opt-in for '582 development no later than shortly after the Ph1/2 update. On competitive positioning, IONS framed the Angelman market as a market big enough for two players and did not opine on molecule differentiation vs Ultragenyx's (RARE) GTX-102. RARE will have expansion cohort data on GTX-102 in 1H24. We note IONS has not published preclinical data on ION582 nor ASO sequence and potency to draw comparisons vs GTX-102. On dosing, Ionis is dose-ranging ION582 and has not disclosed the dose range under evaluation but framed fixed dose as in the range of existing CNS products (wide range, as we note dose for Spinraza is 12mg vs 100mg for Qalsody).

- **'24 detailed data of olezarsen in FCS and Ph3 enrollment pace in sHTG**: IONS plans to file for NDA in lead FCS indication in early 2024, followed by US approval later in 2024 (assuming priority review). IONS is confident around the competitive profile of olezarsen citing sufficient triglyceride (TG) lowering coupled with strong reduction in pancreatitis events and (importantly) no safety issues at the 80mg registration dose. IONS plans to present/publish the detailed FCS data in 2024, noting ACC (medical meeting) or European Cardiology as logical targets. IONS' Ph3 trial Olezarsen in sHTG (one-year study) continues to enroll as of Dec (per ct.gov) thus is positioned to readout in 1H25 at earliest (vs IONS' guidance of late'24 / early'25). Relative to competitor Arrowhead's plozasiran, IONS believes its strong profile and first-mover advantage (several years in sHTG) position the company well.

- **Donidalorsen Ph3 readouts to establish profile in HAE**: IONS will have topline results from registrational Ph3 study (placebo-controlled) in 1H24, followed by mid-2024 readout from a Ph3 switch study (open-label study evaluating patients transitioning from other prophylactic treatments to doni). IONS' Ph2 data indicate doni has best in class potential vs standard of care Takeda's Takhzyro, or more specifically, doni's 90% reduction in HAE attacks in Ph2 on 80mg Q4W dosing vs Takhzyro's 73%/87% reduction in Ph3 on 300mg Q2W/Q4W dosing. We look to IONS' Ph3 results for profile validation of doni: our primary focus is on Q4W data of doni whereas we see Q8W dosing arm (not studied in Ph2) as an optionality for further differentiation vs Takhzyro and emerging oral pipeline candidates.

Acronyms: FCS: Familial chylomicronemia syndrome, CM: cardiomyopathy, PN: polyneuropathy, HAE: hereditary angioedema, ALNY: Alnylam, SQ: subcutaneous, MAD: multi-ascending dose, LTE: long term extension, FDA: US Food and Drug Administration, TBD: to be determined, CNS: central nervous system, NDA: new drug application, sHTG: severe Hypertriglyceridemia, Q2W/Q4W/Q8W: once every 2/4/8-week.

Exhibit 24: Comparisons of ATTR-CM Ph3 trial design
IONS' CARDIO TTRansform is the largest Ph3 CM trial conducted to date

	ATTR-ACT (tafamidis)	ATTRibute-CM (acoramidis)	APOLLO-B (patisiran)	HELIOS-B (vutrisiran)	Cardio-TTRansform (eplontersen)
Baseline					
Enrollment	441	632	360	655	1438
Randomization	3:2	1:1	1:1	1:1	1:1
Trial period	Dec 2013 - Feb 2018	Mar 2019 - May 2023	Sept 2019 - June 2022	Nov 2019 - Feb 2024	Mar 2020 - June 2025
Duration of double-blind period	30 months	30 months	12 months	30 to 36 months (Alnylam expects majority of patient follow-up through 36mo based on enrollment pace)	Up to 32 months (full 32 months for all patients if study progressed to full completion in 2026)
Tafamidis use at baseline	0% / N/A	25%	25% (vs protocol cap ≤30%)	Up to 50% (amended from up to 30%) Alnylam: "somewhat below" the 50% target on tafamidis baseline	Target ~50% but no cap set Ionis: "well balanced" between tafamidis and naïve patients
Tafamidis drop-in protocol	0% / N/A	Drop-in allowed after 12mo	Drop-in allowed anytime	Drop-in allowed after 12mo	Drop-in allowed anytime
Tafamidis drop-in rate	0% / N/A	15% drug, 23% placebo	2-3% drop-in	"Below internal assumptions"	"Very, very low"
# pts on tafamidis at baseline (estimate)	0	158	90	196 - 328	719
# pts not on tafamidis at baseline (estimate)	441	474	270	327 - 459	719
P-value on key efficacy measures at month 30+					
Composite primary endpoint	p<0.001 (Finkelstein–Schoenfeld; sponsor and FDA review) - All-cause mortality, CV hospitalization	p<0.0001 (Finkelstein–Schoenfeld; sponsor) - All-cause mortality, CV hospitalization, change from baseline in NT-proBNP, change from baseline in 6MWT	Not applicable	TBD (Andersen-Gill; sponsor) - all-cause mortality, CV hospitalization, and urgent heart failure visits	TBD (Andersen-Gill; sponsor) - CV mortality, CV hospitalization, urgent heart failure visits

Exhibit 24: Comparisons of ATTR-CM Ph3 trial design
IONS' CARDIO TTRansform is the largest Ph3 CM trial conducted to date

	ATTR-ACT (tafamidis)	ATTRibute-CM (acoramidis)	APOLLO-B (patisiran)	HELIOS-B (vutrisiran)	Cardio-TTRansform (eplontersen)
All-cause mortality	p<0.001 (Finkelstein–Schoenfeld; sponsor) p=0.007 (Kaplan Meier; FDA review) p=0.026 (Cox proportional hazard; label)	p=0.057 (Cochran-Mantel-Haenszel; sponsor) p=0.15 (Cox proportional hazard; sponsor)	Not applicable	TBD	TBD
CV mortality	Not presented, but benefit in all-cause mortality was driven by CV-mortality (FDA review)	p=0.037 (Cochran-Mantel-Haenszel; sponsor) p=0.089 (Cox proportional hazard; sponsor)	Not applicable	TBD	TBD
CV hospitalization	p<0.0001 (Poisson regression; label)	p<0.0001 (Negative binomial regression; sponsor)	Not applicable	TBD	TBD

Source: FDA.gov, company reports

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ITCI: Ph3 Caplyta MDD readout + sales ramp in approved indications

In 2023, ITCI shares outperformed (+36% vs +8% XBI) largely due to Caplyta's strong commercial adoption driven by the late '21 BPD label-expansion. The stock price also benefited from positive Ph3 data for Caplyta in patients with mixed features (with either MDD or BPD). We believe the positive MF study has the potential for label inclusion and also de-risks the pending adjunctive MDD trial readout. Looking to 2024, we forecast Caplyta sales >$650m (>40% Y/Y) supported by strong script trends and room for further penetration in BPD. In 2024 we focus on:

- **Expecting continued strong execution on Caplyta in BPD and schizophrenia** - we view 2024 Caplyta revenue guidance as a key catalyst for the stock. We assume guidance will be provided on the 4Q call, as the company only started providing revenue guidance later in '23. Given that Caplyta reimbursement is largely set, we look to 2024 commentary on pricing gross-to-nets as important to forecasting longer-term net pricing. As Caplyta enters its third full year with the BPD indication in its label, script trends remain strong driven by momentum from investment in S&M to expand the breadth and depth of the prescriber-base. Additionally, management's commentary on incremental improvement in payer coverage quality – with most of BPD being commercial insurance we look for any signs of GTN weakening in exchange for strong volume offset. We estimate the majority of Caplyta sales to continue to come from bipolar disorder (70%/30% BPD/schizophrenia split) since the category is less competitive and less managed than schizophrenia.
- **Ph3 MDD Caplyta readouts for label expansion** – Caplyta's two parallel Ph3 trials in adjunct MDD (Study 501 and 502) will topline data in 1Q and 2Q that will support an sNDA. Our high (70%) POS for caplyta in MDD is anchored by 1) numerous positive studies conducted by atypical antipsychotics in MDD, including AbbVie's (covered by BofA research analyst Geoff Meacham) Vraylar , 2) a positive Ph3 MF data in MDD patient subgroup. Also, we believe Intra-cellular will be in a position to communicate path forward for mixed features (study 403) after regulatory interactions, but forecast zero revenue in 2024 on our base case assumption that an additional trial is likely necessary. We forecast Caplyta reaching peak sales of ~$1.2bn in depression, inclusive of both the MDD and mixed feature markets.
- **Pipeline updates: deuterated-luma trials initiating 1H24 + LAI formulation** – in 2024, a key area of focus will be pipeline execution, including Ph2 trial initiations for deuterated-luma in three indications: generalized anxiety disorder, Alzheimer's agitation and Alzheimer's psychosis. Proof-of-concept

data from all three trials will determine indication prioritization and timing/size of future trials. Deuterated-luma is formulated as an oral disintegrating tablet for sublingual administration and is expected to have a favorable therapeutic index in the geriatric population by expressing more parent compound. We believe the ADA indication is partially de-risked by the approval of Rexulti (similar MoA) and the ADP is partially de-risked by muscarinics (which are antipsychotics that have shown some efficacy data in that population). We're also looking for LAI ph1 trial initiation in 1H24 where the goal for dosing is treatment duration > 1 month (most common LAI dosing interval).

Acronyms: MDD: major depressive disorder; BPD: bipolar depression; MF: mixed features; GtN: gross-to-net pricing; POS; probability of success; sNDA: supplemental new drug application; luma: lumateperone; LAI: long-acting injectable; ADA: Alzheimer's Disease agitation; ADP: Alzheimer's Disease psychosis; MoA: mechanism of action.

JAZZ: oxybate defensive & pipeline wildcards

In 2023, JAZZ was an underperformer (-23% vs +5% DRG) largely due to the emergence of competition to Jazz's oyxbate business and no offsetting pipeline updates. Heading into 2024, we believe it will be important for Jazz to demonstrate sustained growth of its longer-duration assets (Xywav-IH, Epidiolex, Rylaze), generate some pipeline success and consummate a high-quality business development transaction. At Jazz's current '24 P/E and EV/EBITDA multiples both <7x, we believe the stock trades at floor value and we see risk/reward meaningfully skewed to the upside.

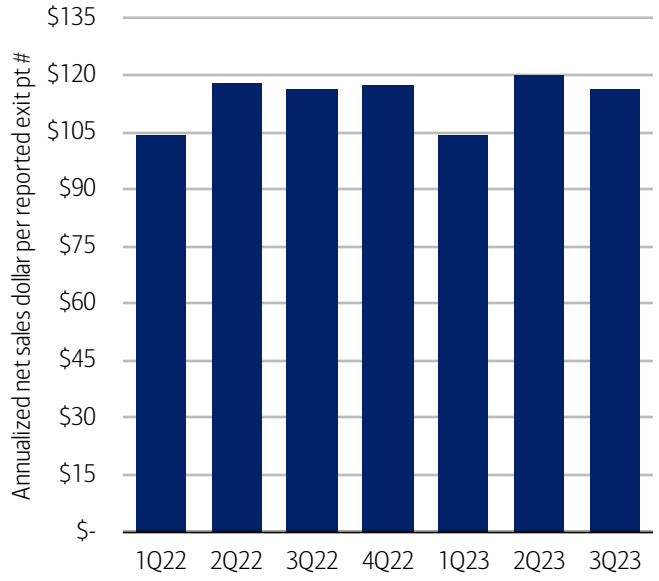
- **Jazz has several late-stage data cards in 2024-25:** Near-term, we expect Jazz to report Ph2 data for JZP150 Ph2 for treatment of PTSD (est. Jan 2024 readout) and JZP385 Ph2b for essential tremor (1H24). Both the '150 and '385 programs are high risk/high reward as we previously published in our pipeline deep dive (full analysis here). We are most confident zanidatimab Ph3 in 1L HER2-expressing GEA cancer (readout 4Q24/1Q25) can readout positively (based on prior data). We forecast zani conservatively reaching $600m in global nominal sales but we believe the GEA indication could approach $1bn (depending on strength and breadth of data).

- **We model stable outlook for oxybate in 2023-25:** We continue to see stable 2023-25 oxybate revenue driven by Jazz's follow-on Xywav brand + better than expected net pricing (competitor Avadel expects $120k steady-state pricing). While there are Xyrem authorized generics commercially available, those products have had limited impact (est. 20% pt share) likely owing to high royalty owed back to Jazz. In '24E, we expect AG generics + branded competitor (Lumryz) will continue to take share from Xyrem but we expect Xywav growth to partially offset with growth in both its approved indications. We expect Jazz to exit 2024 with branded Xyrem largely phased out and all of Jazz revenue coming from Xywav/ AG royalties.

- **Growth ex-oxybate is key, focus on Epidiolex + Rylaze:** Other important Jazz growth drivers include Epidiolex and Rylaze where cons projects peak sales of $1.2bn and $770m, respectively, versus 2023E ~$840m and ~$400m, respectively. While Rylaze has offered more upside surprise since launching, we believe it is imperative that both brands continue to grow as they contribute ~75% share of 2023-27 growth (in our forecast). With more stable oxybate dynamics, we view Epidiolex/Rylaze as key for Jazz to grow revenues in the mid-SD in the 2023-27.

Acronyms: 1L: first-line, HER2: biomarker, GEA: gastroesophageal adenocarcinoma, AG: authorized generic, SD: single digit.

Exhibit 25: JAZZ's sodium oxybate franchise roughly ~$120k / pt
Based on reported exit patient number, we depict annualized net sales / pt



Source: BofA Global Research estimate, company reports

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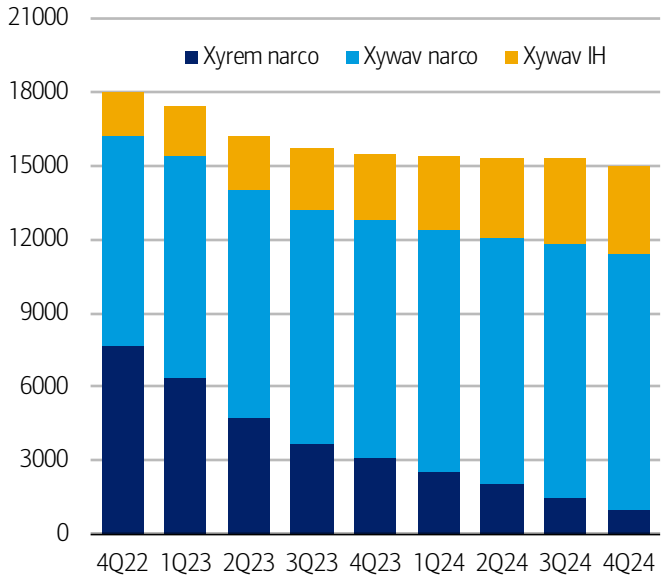
Exhibit 26: Xyrem narco erosion partially offset by Xywav narco + IH
We forecast '# of pts on oxybates thru 4Q24 based on current rate of erosion



Source: BofA Global Research estimate, company reports

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LYRA: Ph3 ENLIGHTEN key milestone in CRS portfolio

In 2023, Lyra was a notable outperformer (+65% vs. +8% XBI) with the stock currently trading at highs reached after the Ph2 BEACON study (LYR-220 for post-surgical CRS) results were announced (September). We view LYRA as a deeply discounted stock relative to its large potential TAM's with its chronic rhinosinusitis treatments. In 1H24, LYR-210 will report pivotal Ph3 data in the pre-surgical CRS population and (earlier) Ph2-profile suggests (to us) competitive differentiation as the only single-use implant with 6-months of CRS symptom relief (vs. daily steroids sprays/ surgery). In 2024 we focus on:

- **Ph3 Enlighten-1 readout 1H24 is the key company catalyst event:** The Ph3 Enlighten program consist of two registrational trials (Enlighten-1 and -2), comparing LYR-210 in polyp and non-polyp CRS pre-surgery patients versus sham control. In Aug. 2023, Enlighten-1 completed patient enrollment while enrollment completion for Enlighten-2 is expected by 2H24. The Ph3 primary endpoint will be baseline changes in CRS symptoms (3 cardinal symptoms) measured after 24-weeks of treatment. In a prior Ph2 study (LANTERN), LYR-210 did not reach stat sig benefit on the 4-week symptom score but did show benefit at weeks 8-16 and the effect was maintained over 24-weeks. The LANTERN results underpin our confidence in the Enlighten program and are the reason we model a 70% POS.

- **Lyra is focused on CRS implants with long-acting efficacy:** Lyra is developing two steroid-eluding implant meshes, known as LYR-210 and LYR-220. Both Lyra meshes are being developed as treatments for chronic rhinosinusitis but at different stages of the disease. While steroid nasal sprays are widely used, the meshes were developed to reside in difficult (to reach) areas of the nasal cavity and provide a prolonged 6-month durability benefit. If approved, both Lyra meshes would be administered as part of an in-office procedure. We forecast nominal peak sales for LYR-210 at ~$670m with an assumed 70% POS; of the 13m prevalence CRS patients, we estimate ~850k would be candidates for LYR-210 (these are pts that have exhausted the use of steroid sprays).

- **Lyra has cash runway into 1Q25:** On its 3Q23 update, Lyra updated that its ~$100m in cash should provide sufficient funding to operate the company into 1Q25. We view Enlighten-1 as a high impact catalyst, which if positive would expand the company's options to bring in capital ahead of the Enlighten-2. Other programs that could warrant funding /investment is LYR-220 following the positive Ph2 BEACON trial. Lyra plans to meet with the FDA to discuss the BEACON results and we'd view positive Enlighten trial results as reading across to '220 in the post-surgical indication.

Acronyms: CRS: chronic rhinosinusitis, POS: likelihood of success.

OCS: multiple pipeline readouts are key upside drivers

In 2023, Oculis modestly outperformed (+11% vs. +8% XBI) relative to the biotech index driven by two favorable Ph3 readouts for OCS-01 in DME (diabetic macular edema; stage 1) and treatment of pain and inflammation associated with post-ocular surgery. In 2024, we expect investors to focus the mid-'24 Ph2b readout of OCS-02 (anti-TNF) in dry eye as well as several other smaller pilot studies: (1) OCS-02 Ph2b trial in uveitis patients (est. 2H24 readout), (2) OCS-01 study in two forms of CME – uveitic macular edema and post-surgical macular edema est. readout in 4Q24, and (3) OCS-05 Ph2a study in acute optic neuritis patients est. readout in 4Q24.

- **OCS-01 for post-op pain expected to complete second pivotal + move to NDA:** in 2024, we look to topline data from a second confirmatory Ph3 evaluating OCS-01 post-op pain that would lead to an NDA filing and 2025 approval. While the post-op pain indication is relatively small (~$100m NPV or $3/sh), we note it will likely be Oculis' first commercial indication and allow the company to start building out its commercial infrastructure prior to the DME indication which will have pivotal data in 2025. DME represents the biggest value driver for the stock, and we model $10/shr (80% POS). The value prop of OCS-01 in DME is topical steroid delivery that could play in the watch-and-wait or be used in combination with VEGF therapies in more advanced patients.

- **OCS-02 Ph2b in dry eye is an important de-risking event:** Ahead of mid-'24E Ph2b readout for OCS-02 in dry eye, we model a conservative 50% POS mainly due to some limitations in the supportive data. Previously, NVS studied '02 in a Ph2a POC study which demonstrated a statistically significant improvement in DED (dry eye) symptoms but was not evaluated for improvement in ocular signs of disease (FDA requires improvement in both measures). In Ph2a, OSC-02 was evaluated in patients with ≥ 6 months history of DED and showed statistically significant improvement in subjective outcomes (4.3-point placebo-adjusted improvement in Global Ocular Discomfort Score) while improvement on objective secondary endpoints such as physician graded conjunctival hyperemia, corneal staining, Meibomian gland assessment, and tear film osmolarity were more muted. To secure approval, OCS-02 will need to demonstrate improvement in both signs and symptoms of disease thus we see Ph2b as an important de-risking event. Our $7/shr contribution from OCS-02/DED assumes nominal peak sales are more niche, reflecting market fragmentation.

- **Multiple early proof-of-concept trials**: Earlier stage assets/indications in Oculis' clinical-stage pipeline include (1) OCS-02 in uveitis patients (Ph2 est. 2H24 readout), (2) OCS-01 in two forms of CME – uveitic macular edema and post-surgical macular edema (Ph2 est. readout in 4Q24). OCS-01 is being evaluated in these patients based on the presumed therapy overlap with DME, and (3) OCS-05 in acute optic neuritis (Ph2a est. readout in 4Q24). Given that these are proof of concept studies, we currently ascribe little value to each individually (aggregate $1/sh or <$50m equity value).

Acronyms: TNF, VEGF: drug targets, NDA: new drug application, CME: cystoid macular edema

OGN: '24 guide, with focus on margins + topline

In 2023, OGN meaningfully underperformed (-48% vs +5% DRG) relative to the pharma index driven by margin pressures on the business. As Organon faces a 2027 LOE on US Nexplanon (biggest market), we believe the company needs to be active in BD but dividend commitments and modest rising net-debt leverage have been impediments to deal making. In 2024, we look to whether Organon can delivery mid-SD revenue growth (on ex-Fx basis), realize an uptick in US biosimilar Humira sales and whether '23 Nexplanon sales growth slowdown is a trend or one-off.

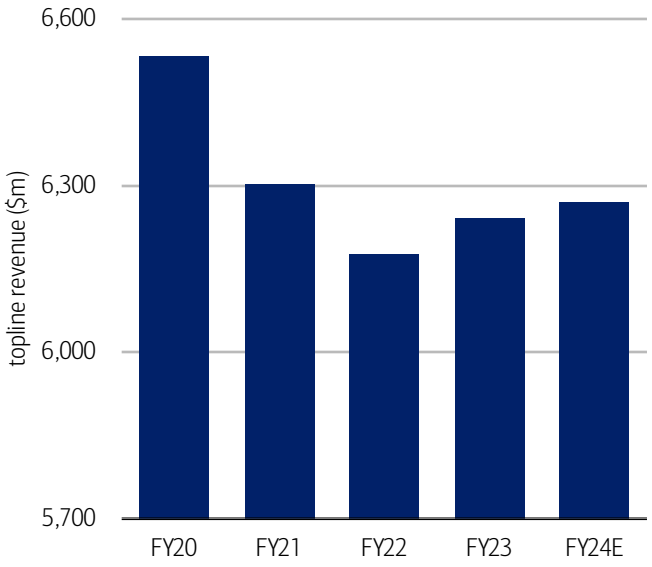
- **Women's health biz has short-term tailwinds** – Organon expects its global Nexplanon business to grow high-SD in 2024 and believes the drug can achieve a $1bn run-rate in 2025. Growth of Nexplanon was slowed to +6% Y/Y in 2023 due to foregoing a price hike, lower pricing due to volume from 340b channels, and lack of participation in Mexico tender, while management's 2024 outlook includes ~$40m of benefit from first-time geo expansion (Asia/Africa) and shifts in customer buying patterns providing a +5% tailwind to Y/Y growth. By our estimate, US Nexplanon has ~33% TRx share of the LARC category vs. 30% share in 2022. On the fertility business, Organon's global franchise remains relatively niche with '24 growth sources expected to be China-tailwinds and recent onboarding of new customer in US, but OGN's ability to capture increased volume share to some extent is due to lowering pricing. Headed into 2024, management expects OGN fertility products to be the preferred brands in a significant percentage of covered lives in the US.

- **Capital deployment focused on M&A and driving organic growth** – In 2024, OGN expects to work towards reducing leverage, investing in the existing portfolio to drive organic growth and engage in business development to acquire assets that can help OGN improve its growth profile. Given free cash flow has compressed, we would not be surprised to see OGN lower its annual dividend outlay (in absolute terms) given target has been to match 20% of FCF (stated policy at spin), but compressing EBITDA/FCF is not a good recipe for levering up the business. As such, we would not expect OGN to take on a massive amount of leverage unless a target acquisition enabled a rapid path to de-leveraging. We view Organon's recent deal with Eli Lilly to commercialize Emgality in Europe for $50m upfront (+ sales-based milestones) as the type of deal that adds minimal balance sheet pressure. BofA Global Research's large pharma team forecasts Emgality EU sales of $329m by 2028 vs. $212m in 2024.

- **Fx neutral in 2024 & focus on Emgality impact on margins:** We forecast 2024 EBITDA of $1.94bn (30% adj EBITDA margin) versus cons $1.95bn (32% adj EBITDA margin) which compares to 2022-23 EBITDA margins of 31-34%. In 2023, OGN lowered its adjusted EBITDA margin to reflect the impact of Fx on revenue, unfavorable product mix and timing of manufacturing costs. The evolution of OGN's gross margins will be an area of focus in 2024 guidance. As we look at various push/pull factors, volume growth has generally been a tailwind for OGN offsetting various headwinds faced since 2020, including China VBP (volume-based procurement), price, supply/other, and FX (Exhibit 27; Exhibit 28). Based on current Fx spot rates for OGN's most heavily ex-US currencies, we forecast neutral Fx 2024.

Acronyms: BD: business development, SD: single digit, LARC: long-acting reversible contraceptives, TRx: total prescription

Exhibit 27: Revenue returned to growth following 3 years of decline
Continued volume growth will be key to arresting topline revenue decline



Source: BofA Global Research, company reports

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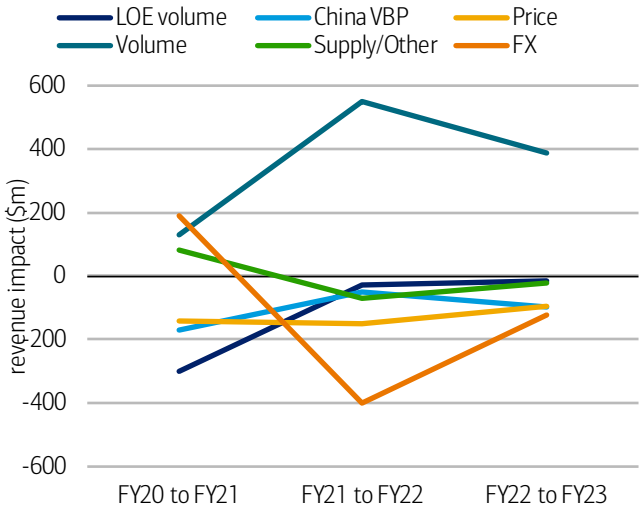
Exhibit 28: Volume growth partially offsets LOE, VBP, pricing, supply, FX headwinds
OGN base business has consistently faced headwinds to growth



Source: BofA Global Research, company reports

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PCVX: Ph2 VAX-31 in adults (potential category killer)

In 2023, PCVX was an outperformer (+32% vs +8% XBI) following VAX-24's positive Ph2 study in elderly adults. Combined, VAX-24 demonstrated highly favorable Ph2 studies compared to Pfizer's PCV in adults and in elderly subjects. With VAX-24, Vaxcyte has a vaccine that looks to offer the broader serotype coverage of any pneumococcal vaccine in clinical development while the company's recently initiated Ph1/2 for VAX-31 could expand coverage against all pathogenic serotypes. The pneumococcal vaccine category is ~$8bn in global revenue and has historically been a winner-takes all market for the vaccine offering the broader disease protection. In 2024 we focus on:

- **VAX-31 Ph2 immunogenicity data in 2H24** – the most impactful 2024 catalyst for PCVX stock will be Ph2 data from an ongoing trial assessing safety and immunogenicity of VAX-31 compared to (Pfizer's) standard of care Prevnar-20 in adults. PCVX's second-gen VAX-31 is based on the same underlying technology as VAX-24 and looks to provide direct coverage against 95% of invasive pneumococcal disease circulating in US adults (+ cross protection against the remaining strain). If the VAX-31 study is positive, we view the Ph2 adult study as highly predictive of Ph3 success as well as success in the infant/pediatric setting. The VAX-31 Ph2 portion will recruit ~1,000 adults and evaluate three doses of VAX-31 against PCV20 evaluating safety and head-to-head immunogenicity. While there is preclinical validation for VAX-31 in white rabbit model (same model used to evaluate VAX24) demonstrating coverage against all 31 strains, we suspect investors will remain skeptical about the ongoing clinical trial given the industry's historical challenges improving the scope of serotype coverage. In the context of a Ph2, we view a win as demonstrating non-inferiority against most of the 20 shared strains and hitting statistical thresholds for 11 incremental strains; for strains that miss, a solid point estimate would be fine as confidence intervals should tighten in larger Ph3 trials.

- **Feedback on CMC plans to support VAX-24's Ph3 trial** – in 2024, Vaxcyte plans to initiate registrational Ph3 trial evaluating VAX-24 in adults with topline data in 2025. Heading into 2024, Vaxcyte has already reached FDA alignment on key parameters where the primary endpoint needed for approval is head-to-head immunogenicity while trial initiation is primarily gated by alignment regarding CMC

strategy for final drug product. An FDA meeting early next year will provide alignment on manufacturing strategy and final trial design to support a trial initiation. We see VAX-24 as potentially best-in-category with Ph3 data in 2025.

- **Competitor updates, plans for earlier-stage pipeline** – Heading into 2024, Vaxcyte is well-funded with cash of ~$1.4bn to support late-stage PCV pipeline. We don't anticipate any major competitor updates on higher valency PCV programs next year, with the exception of Ph2 infant data from GSK/Affinivax's AFX3772 which could be in a position to report data by year-end if the trial is restarted (TBD). Next year, we look for timeline updates for Vaxcyte's preclinical candidates: 1) VAX-A1 for the prevention of strep A and 2) VAX-PG for the prevention of periodontitis. We view both candidates as high risk given lack of outlined clinical development path but both markets could be significant based on prevalence.

Acronyms: PCV: pneumococcal vaccine; stat. sig: statistical significance; NI: non-inferiority; PCV20: Prevnar-21; FDA: food and drug administration; CMC: chemistry, manufacturing and controls, TBD: to be determined.

PROK: Ph2 bilateral data; update on potential Ph3 interim

In 2023, PROK shares underperformed (-74% vs +8% XBI) largely on timeline delays and a large holder liquidating its position in PROK. The stock was also impacted by the evolving CKD standard of care landscape where early efficacy data from GLP-1 kidney outcomes trial in type 2 diabetes patients suggests renal benefit on a composite endpoint. 2024 will offer detailed data on GLP-1 impact on kidney function including eGFR measures which we believe investors are looking at as a competitive threat to REACT's market opportunity. We also look for Ph2 data for first bilateral REACT dosing in stage 3/4 CKD patients and an update on the possibility of interim data from registrational Ph3 Proact-1. We view 2024 as a catalyst-light year given the uncertainty of the Ph3 interim, and downgrade PROK to Buy from Neutral with our $2 PO reflecting a more conservative nominal peak sales outlook (given competitive uncertainties).

- **Bilateral REACT-007 Ph2 data** – in 2024, ProKidney expects Ph2 data for bilateral REACT dosed in stage 3/4 CKD patients with baseline eGFR 20-50 mL/min. We are focused on eGFR benefit as a measure of renal function where patients with CKD have an average eGFR decline of ~4/year. We expect efficacy that is it at least in-line with (and potentially better given bilateral dosing) prior Ph2 single dosing trial which demonstrated -6% average yearly eGFR slope, an improved benefit compared to SOC. We view -007 as an important update as it will provide read-through to pivotal Ph3 REACT dosing (also doses bilateral; vs prior Ph2 only dosed one kidney).

- **Update on potential Ph3 Proact-1 interim read-out** – in 2024, we look to enrollment updates on the US registrational proact-1, blinded sham-controlled study of ~600 stage 4 CKD (GFR 20-35 ml/min) patients. The pause in Proact-1 is expected to conclude in 1H24 after manufacturing quality deficiencies are addressed. PROK will be reviewing options around any interim analysis, which would be dependent on enrollment speed. At the moment, it is unclear if PROK will be able to deliver an interim readout prior to end of cash runway (4Q25).

Acronyms: CKD: chronic kidney disease; (e)GFR: (estimated) glomerular filtration rate; SOC: standard of care

RLAY: PI3K-alpha data in mid/2H24 key stock catalyst

In 2023, Relay (RLAY) underperformed biotech peers (-26% vs +8%) as initial clinical data of RLY-2608 (PIK3CAi; value driver) in 2L+ metastatic breast cancer (mBC) came in below Street's expectation. Nonetheless, RLAY continues to progress two lead programs (PIK3CAi, FGFR2i) through dose expansion trials and expects to provide clinical data updates for both in 2024. Trading at $400-500m EV, we believe the Street is mainly giving RLAY credit on cash and FGFR2i while expectations for PIK3CAi (RLY-2608) are relatively low even though '2608 targets a much larger commercial opportunity. In 2024, we see '2608 updates as key to stock upside.

- **RLY-2608 in 2L+ HER2-, PIK3CA-mutated, breast cancer**: RLY-2608 is aimed at offering better efficacy (durability; PFS) and safety relative to current targeted therapies approved for 2L+ PIK3CA-mutated mBC (metastatic breast cancer), namely Novartis' Piqray and AstraZeneca's Truqap. In 2023, we believe investors benchmarked initial Ph1 data (+ fulvestrant) vs. Piqray/Truqap on response rate (ORR): 1 PR out of 11 pts who received RP2D (600mg BID) and had at least one scan (or 9%) vs 20%'s range from Piqray/Truqap, though we note RLAY's Ph1 sample size (n) was small and one-fourth of pts only had one scan in (short duration of follow-up). On clinical benefit rate (CBR) which is a proxy for durability of benefit, RLY-2608's initial data looked encouraging with 6 out of 7 pts achieved CBR (86%) among pts on RP2D who had at least 6-month follow-up vs 56% Truqap (Ph3) and 46% alpelisib (Ph2 ByLIEVE), though RLAY's Ph1 data was based on small sample size thus will need to be confirmed in subsequent data cuts. On balance, while initial Ph1 data were not perfect, we believe RLAY's 2608 encouraging CBR rate (albeit small n) bodes well for RLAY's next update in 2024 (mid/2H24), where durability of efficacy will be the focus. The '24 update will feature CBR data on 17-20 patients on RP2D. While RLAY has not confirmed whether there will be PFS estimates, we believe there will be enough follow-up for RLAY/investors to gauge PFS considering 17 pts enrolled as of July datacut would have around one-year or longer additional follow-up in next update, vs ~7mo PFS from Piqray/Truqap. Ultimately, durability by PFS will be key to establishing a differentiated profile vs Piqray and Truqap. Lastly, RLAY also has a second PIK3CAi in early Ph1 development (RLY-5836), though management had noted the bar to replace RLY-2608 would be high.

- **RLY-2608 in 1L HER2-, PIK3CA-mutated, mBC**: Roche's recent positive Ph3 readout of Inavolisib (PIK3CAi) in 1L HER2- PIK3CA-mutated mBC has effectively expanded the addressable market for the class by ~4x (est. ~$5bn 1L opportunity vs $1-1.5bn for 2L+). Inavolisib triplet with palbo (CDK4/6) and fulvestrant hit PFS primary endpoint (15mo mPFS vs 7.3mo palbo/fulvestrant doublet; HR=0.43) and showed a positive OS trend (HR=0.64) at immature data in Ph3 data, suggesting the triplet regimen could become the standard of care in that pts population. RLAY plans to initiate a Ph1 triplet cohort by YE23 evaluating RLY-2608 with ribo (CDK4/6) and fulvestrant in 2L+ mBC (primary objectives: safety and combinability). While initial data disclosure of RLY-2608 triplet is likely a 2025 event, we expect investors to focus on enrollment pace and management's commentary on dose escalation experience. Nonetheless, we expect investors to look to RLAY-2608's update in 2L+ mBC to gauge competitiveness vs inavolisib/fulvestrant available data in 2L+ setting (Ph1: 19% ORR, 48% CBR). Assuming RLAY can initiate a Ph3 trial in 2025 and 3-4 years to run a Ph3 to PFS primary (inavolisib Ph3 timespan), we estimate potential 1L launch in 2029-2030 (or 4-5 years behind Roche).

- **Lirafugratinib (RLY-4008) in FGFR2-altered solid tumors**: for lira (RLY-4008) in 2024, we expect to see Ph2 pivotal data in CCC (bile duct cancer) and updates on dose-expansion data in broader FGFR2-altered tumor types outside of CCC. RLAY plans to pursue a tumor-agnostic label for lira, and we look to 2024 data and regulatory updates (pending discussions with the FDA) on breath of a potential tumor-agnostic label, for example, agnostic to tumor types within a specific FGFR2

alteration type (eg FGFR2-fusion), or agnostic to FGFR2 alterations (eg fusion, amplification, and/or mutations) within the context of specific tumor type(s), or broadly agnostic to any FGFR2 alterations regardless of tumor types. Initial non-CCC data of lira (see report) were most robust among FGFR2-fusions whereas its therapeutic potential in other alterations is TBD. RLAY has indicated 30% and 6mo+ duration of response as a moving target that may support tumor agnostic approval. We estimate $400-450m nominal peak sales for lira in more de-risked FGFR2-fusion solid tumors (including CCC).

Acronyms: PI3K-alpha/PIK3CA, FGFR2, CDK4/6: drug targets, i: inhibitor, L: line of therapy, PFS: progression free survival, Ph: Phase, RP2D: recommended Ph2 dose, BID: oral twice daily, ORR: objective response rate, CBR: clinical benefit rate, OS: overall survival, pts: patients, TAM: total addressable market, TBD: to be determined, FDA: US Food and Drug Administration.

ROIV: updates on FcRn franchise and cash deployment

Roivant (ROIV) outperformed biotech peers in 2023 (+40% vs +8% XBI), driven by positive clinical updates on its FcRn franchise (IMVT-1402 and batoclimab) via subsidiary Immunovant's (IMVT) and cash infusion from sale of its TL1A asset. At ~$10bn market cap fully diluted, the Street is mainly giving ROIV full credit on net cash (~$6.5bn pro forma net cash) and 55% ownership of IMVT (~$3.3bn). In 2024, our focus is mainly on ROIV's strategy on cash deployment, clinical progression of IMVT-1402, and clinical readouts on batoclimab. Positive development of the FcRn franchise may drive upside to ROIV shares, though non-controlling interest (ROIV owns 55% of IMVT) could limit the magnitude of upside to ROIV. Conversely, ROIV is not yet profitable with operating cash burn in the range of $800-900m last 12mo, and continued cash outflow could lead to the Street's discounting ROIV's valuation on cash.

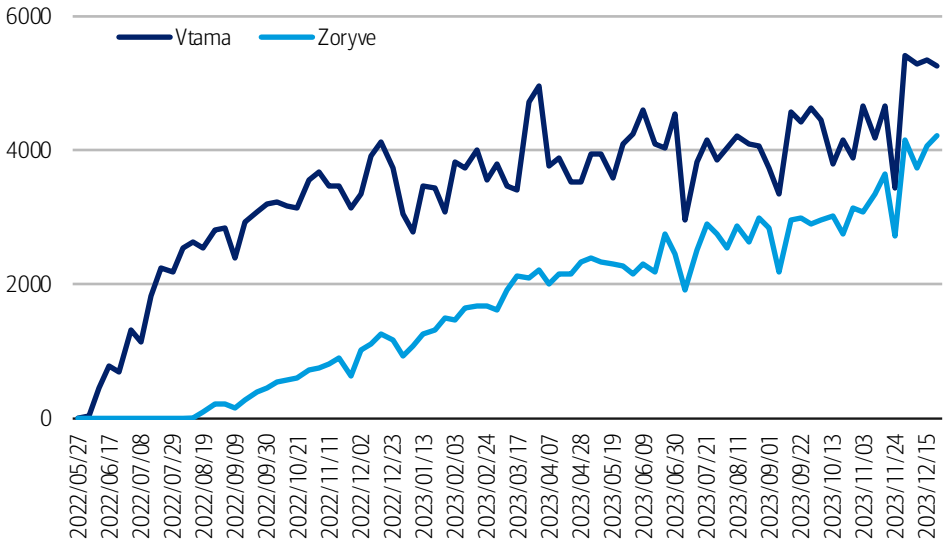
- **Strategy on cash deployment**: ROIV exited FY2Q23 (Nov'23) with ~$7bn pro forma gross cash (~$6.5bn net cash) which factors in IMVT's follow-on offering in Oct'23 and proceeds on sale of Telavant. ROIV has discussed business development and returning capital to shareholders as possible venues for capital deployment, though the company had not provided any concrete plan/timeline and noted on last earnings call it would be "patient" on capital deployment. With brepo program now discontinued in lupus and VTAMA launch slowing, ROIV's setup in 2024 is levered to the company's strategy on capital deployment and updates on the FcRn franchise. Lastly, we will look to ROIV's burn rate in 2024 vs $200-250m cash burn per quarter last year (excluding any equity financing or cash inflow from asset sale).

- **Updates on IMVT-1402 and batoclimab**: as noted in greater detail in our IMVT write-up above, we will look to Ph2b bato data in CIDP (chronic inflammatory demyelinating polyneuropathy) to inform dose-response and value proposition of deeper IgG reduction (in CIDP). For Ph3 readout in MG (myasthenia gravis) in 2H24, we will look for Ph3 repeating similar magnitude of effect size as prior Ph2. On IMVT-1402, our focus is on IND clearance and disease prioritization of the asset.

- **Tracking VTAMA sales ramp**: ROIV's VTAMA is a topical cream approved for the treatment of psoriasis. VTAMA script growth had moderated after year 1 of launch. While VTAMA TRx volume appears to have trended up in December, we note TRx from overall topical psoriasis and competitor product (Arcutis' Zoryve) also increased in the same period (Exhibit 29). As such, we still need more weekly data to gauge whether VTAMA script trend has returned to growth vs transient market dynamic / script fluctuation. ROIV plans to submit an sNDA for VTAMA in atopic dermatitis (AD) in 1Q24, which would position a '25E label expansion into AD.

Acronyms: TL1A, FcRn: drug target, IQVIA: prescription database, TRx: total prescription, sNDA: supplemental new drug application.

Exhibit 29: Script trend (TRx) of key topical launches in psoriasis
VTAMA script growth has slowed after 1-year into launch



Source: IQVIA NPA June 2022 - Dec 2023

BofA GLOBAL RESEARCH

TARS: looking for Xdemvy scripts to translate to cons revenue upside

In 2023, TARS outperformed (+40% vs +8% XBI) relative to the biotech index. We attribute TARS' '23 performance to the timely approval of Xdemvy as the first FDA approved therapy for demodex blephartitis as well as favorable early launch updates. In 2024, we expect TARS' to trade around Xdemvy launch updates as well as updates from the company's Ph2-stage pipeline (more below):

- **Xdemvy launch is central focus in 2024**: we look to Xdemvy (demodex blepharitis) launch as the key update to unlocking TARS shareholder value in 2024. Our focus will be on volume trends and the drug's progression to steady-state net pricing. Xdemvy is an acute use and possibly periodic-use (ever couple years) drug, thus there are limited launch comps. Further, Tarsus is building out the therapeutic market for demodex blepharitis, even though diagnosis is easy and commonplace. We view Novartis' Lamisil for onychomycosis as a good comp having reached >$1bn in peak revenue (more than 15 yrs ago) for the fungal condition (Xdemvy 8w course vs. Lamisil 90 day). So far, Xdemvy weekly scripts are 2350 and 1300 per IQVIA and Symphony during week ending 12/1, respectively; the IQVIA number is closer to 1700 after applying a 27% reduction per IQVIA's prior over-statement. While the script numbers are not perfect and tracking Xdemvy's four specialty pharmacies will take some time, we believe the Symphony numbers (most conservative) are encouraging considering an average 1700 weekly are implied in cons $55m 2024 sales (at 66% GTN deduction). We believe a key catalyst for TARS stock will be actual reported revenue, which should provide investors with more confidence that payers will cover the drug which carries a $1850 per course list price. Mgmt has indicated 80% GTN deduction at launch progressing to 50% steady state.

- **Ph2 TP-04 rosacea data; big but tough market**: TARS is evaluating TP-04 (topical lotilaner gel) for treatment of PPR (popular pustular rosacea) in a 30 patient Ph2 12-week study two-arm study (2% drug vs. pbo) with a focus on safety and a number of exploratory efficacy endpoints (all listed as secondary endpoints). TP-04 is being advanced on the hypothesis that demodex mites are prevalent on the skin and may contribute to inflammatory response associated with disease. The rosacea market is potentially large with 18-28% of 16m US prevalence suffering PPR disease type, but recent brand rosacea launches have been underwhelming. Soolantra (generic ivermectin) is an anti-parasitic achieved $200m peak IQVIA gross sales and is now generic. Tarsus' hope is to develop TP-04 for rosacea with unique label claim differentiation vs. Soolanta though we need to see Ph2 data before we can speculate on any unique and differentiable claims.

- **Ph2 lyme prevention – looking to validate partnership candidate**: Tarsus is evaluating TP-05 as an orally dosed lotilaner for prevention of lyme disease. In 1Q24, Tarsus plans to report initial Ph2 data from CARPO, a tick-killing study with various safety-focused primary efficacy endpoints such as changes from baseline in AEs, hematology lab tests, ECGs, QTC interval, and QRS interval. The Tarsus approach could in theory facilitate periodic monthly dosing of an oral agent during tick season in high-risk areas. The Tarsus approach differs from the vaccine approach (studied by Pfizer) though both likely share a similar Ph3 development pathway (Pfizer's Ph3 includes 9000 subjects 2.5 yr evaluation), thus Tarsus has long viewed the TP-05 lyme opportunity as a partnership opportunity once it gets beyond Ph2 tick killing or Ph2b de-risking events. Per mgmt, we look for high tick-kill rates in Ph2 along with a pristine safety profile.

Acronyms: IQVIA: prescription database, GTN: gross to net, pbo: placebo, AE: adverse event, ECD: electrocardiogram, QTc, QRS: heart rhythm measures

TEVA: '24 guide + key pipe updates (OLZ-LAI, TL1A)

In 2023, TEVA modestly outperformed (+15% vs +5% DRG) relative to the pharma index. We attribute TEVA strength to favorable 3 factors: 1) strong brand performance – Austedo and launch of Uzedy LAI; 2) overall business has performed better than expected vs. concerns at the start of the year around biosimilar Humira contribution; and 3) litigation overhang removal – in '23 the key update was around the DOJ's price fixing probe which was settled. Heading into 2024, we look for indications TEVA is tracking well against its "Pivot to Growth" targets with growth on both the top and bottom-lines coupled with important progress from the pipeline, notably:

- **Several key late-stage pipeline readouts in '24E**: We look to Ph3 data for TEVA's olanzapine LAI (TEV-'749; data 2H24) and Ph2 data for the anti-TL1A program (YE24). Key to the '749 value-proposition will be safety differentiation relative to Lilly's marketed Relprev, which is also an OLZ-LAI but never gained meaningful market traction due to a safety boxed warning for post-injection delirium/sedation. Teva believes it can avoid the post-injection side effect based on its formulation technology and the company has injected >900 patients with zero events vs. pre-agreed target of 3500-3600 injections without an event to secure approval without the safety warning. We like the '749 commercial opportunity if '749 can achieve safety differentiation given olanzapine is widely used oral (1% oral share vs. 11% oral share in 2022). More important will be TEVA's Ph2 data update for TEV-48574, the companies 50-50 partnered TL1a antibody for treatment of IBD disorders. Teva believes '48574 its anti-TL1A can achieve greater potency and reduce the circulating levels of TL1a to a greater degree than competitor molecules. We expect investors to focus on efficacy, though the initial 14-week induction efficacy measures of remission (UC) and endoscopic response (Crohn's pts) are unlikely to differentiate from competitor TL1a's which were at the high end of

biologics in those settings, thus we see 2024 as more of a progress milestone towards longer-term value creation with the asset.

- **US generics offer an interesting mix of new product opportunities in '24E**: Heading into 2024, we have visibility around 3-4 new product opportunities: 1) generic Revlimid which contributed est. $1.4bn 2023 IQVIA gross sales vs. ~$400m in 2022 is expected to be a tailwind in '24, per management, 2) Generic Sandostatin LAR is expected to launch in early '24 and so far TEVA is the only Gx mfg to receive approval for the $800m net US sales brand; 3) generic Victoza has a settlement to launch alongside Sandoz for the ~$1bn YTD '23 net sales brand; and 4) generic Forteo finally secured approval in 4Q – current market dynamics include 3 competitors with approved generic Forteo (Alvogen/Pfenex, Prasco [authorized generic], Apotex) and another Amphastar (AMPH) with a late-stage pipeline program for a generic Forteo. Last, an early 2024 inspection of partner Alvotech's biosimilar facility is the final gating item to TEVA securing the first interchangeable high concentrate b-Humira, which we see as upside optionality (though commercial upside could be challenging entering late in payer contracting cycle).

- **Austedo looking to shine, with added S&M resources**: In 2024, Austedo will be in its 7th year on the US market having reached $1.2bn in 2023. The VMAT-2 inhibitor market is ~$3bn in sales with Austedo possessing a 40% dollar share. Teva garnered attention at its May 2023 Investor Day providing a target to $2.5bn in 2027 sales which would require a sales acceleration. In 2H23, script growth has been strong (Symphony +37% Y/Y; IQVIA +29% Y/Y) while street forecasts +17% 2024 growth. New marketing investments are expected to benefit the brand starting in early 2024 and improve revenue per patient (adherence, more pts at optimal dose) and facilitate market share gains. Even if management is directionally accurate on its Austedo forecasts, we believe Austedo should drive a favorable mix shift in 2024+ and help the company meet or meet EBITDA targets.

Acronyms: LAI: long acting injectable, DOJ: department of justice, OLZ: olanzapine, VMAT2, TL1A: drug targets, Gx: generic, LAR: long-acting,

VTRS: base biz margins + capital deployment key to '24

In 2023, VTRS underperformed (-3% vs +5% DRG) relative to the pharma index. We attribute the stock's weakness to gross margin pressures facing the business in 2H23 and non-core asset divestiture proceeds that came in at the low end of management's projection range ($3.6bn vs $4-6bn proceeds targeted for planned divestitures) due to the decision to retain commercial rights to Viagra, Dymista and select OTC products which management values at at $1.6bn. In 2024, we expect key areas of focus to be on 1) 2024 financial guidance, 2) return of capital to shareholders (buybacks and dividends), and 3) redeployment of proceeds from divestitures expected to close in 1H24.

- **Capital deployment heavily skewed to shareholder returns:** Management recently announced divestitures which are all expected to close in 1H24 with $2.55bn net proceeds, which we expect the company to re-deploy towards debt paydown bringing company gross leverage closer to 3x, share buybacks and business development focused on specialty brands. So far, Viatris' M&A has been targeted at ophthalmology assets (Oyster Point + FamyCare) though gastrointestinal and derm remain priority TA's. Based on Viatris' shareholder return and leverage targets, we would not expect to see the company engage in large-scale, transformative M&A. When Viatris' announced its plan to divest several non-core businesses, the Chairman indicated the company would return 50% of free cash flow to shareholders (via dividends and share buybacks).

- **2024 pro forma RemainCo:** On the 4Q22 call, Viatris (while not giving guidance) directionally indicated $4.6-5bn as a post-divestiture EBITDA range and the company subsequently retained OTC brands contributing ~$125m in EBITDA. Based on where we see 2023 financial results netting + anticipated contribution of the businesses that will be divested (est. ~$350m EBITDA), we forecast 2024 EBITDA coming in around $4.7bn and see some added downside risks including: 1) 2H23 gross margin pressure carrying over to 2024 – if 2H23 gross margins carry into '24, that represents $140-200m drag to our/cons EBITDA; 2) if base business Y/Y erosion, ex-divestitures, trends similar to prior years this could represent an incremental $100-200m downside. In 2024+, the company expects to generate at least $2.3bn FCF annually considering inflation and FX headwinds excluding transaction costs and taxes associated with divestiture.

- **New product launches expected to be ~$500m annually –** Management expects Viatris to remain on track to deliver $450-550m annually in new product launches. Several products stand out as being important to deliver in 2024 including 1) GA (Glatimer Acetate) Depot – long-acting GA Depot PDUFA date of 3/8/24; 2) possible generic launches [pending approval] for Venofer (iron sucrose), Victoza (liraglutide), and Sandostatin LAR (octreotide acetate); and continued benefit from products launched in '23 including 3) generic Symbicort (Bryena) and generic Vyvanse (lisdexamfetamine).

Acronyms: TA: therapeutic area, OTC: over the counter, PDUFA: FDA action date.

XENE: next steps for '1101-MDD

In 2023, XENE shares slightly outperformed (+17% vs +8% XBI) with the primary catalyst being a Ph2 '1101 MDD (depression) trial readout that was positive (on balance). XENE's primary value driver remains '1101 for treatment of epilepsy and in 2023 XENE offered trial enrollment updates narrowing the timeline for the second confirmatory trial readout in 1H25. We continue to see XENE's Kv channel modulator for epilepsy as an attractive peak sales opportunity (>$1bn). In 2024 we are focused on:

- **2024 should offer clarity on plans to advance '1101 for MDD –** in early-2024, XENE will be in a position to offer detailed plans on how it plans to advance XEN1101 for the MDD indication after an end-of-phase-2 FDA meeting. In a prior Ph2, '1101 demonstrated clinically significant improvement on the primary MADRS endpoint though missed statistical significance due to an unusually high placebo response. What we found encouraging about the Ph2 results was the consistency of '1101 drug benefit across all primary and secondary efficacy endpoints including the SHAPS score for measuring anhedonia. The '1101 Ph2 data were consistent with the signal seen with a prior Kv agent (ezogabine) and '1101's safety/tolerability profile looked relatively clean. While the Ph2 results suggest Xenon could explore even higher dosing (upwards of 25mg), we'd note that having two dose arms could increase the risk of a higher placebo response (in Ph3), thus we are curious which dose(s) management advances in future MDD studies. Per management future '1101 follow-on indications of interest, in order of priority, are MDD and other mood disorders (anxiety), respectively. We currently model 65% POS for 1101 in MDD and US peak sales of $830m.

- **Kv7 epilepsy updates mainly confirming XENE remains on track with enrollment timelines –** in 2024, the focus for 1101's lead epilepsy program will be around enrollment updates, where investors are looking to confirm 1101's X-TOLE2 (FOS) trial is on track for a 1H25 readout. Competitor Biohaven's Kv7 modulator BHV-8000 will also be enrolling patients for its pivotal Ph2/3 trials in focal onset seizures, and we look for competitor timeline updates for clarity around order-of-

entry. As of now, BHV-800's Ph1 data indicates potential differentiation on CNS adverse events though small patient limit quality of cross-trial comparisons.

- **Tracking the epilepsy market; investors skeptical there's room for another blockbuster**: There are 24 approved anti-seizure meds making the FOS market "crowded" with multiple mechanisms alternatives. Generic standards of care are likely to dominant 1L and 2L treatment approaches, but we believe '1101 can become the brand of choice in 3L+, which is a big chunk of the market (20% of 3m US pts cycle through multiple therapies). Key to our view is '1101's differentiation (novel MOA, high degree of efficacy, tolerability and ease of dosing). We look to commercial progress of SK Life Sciences Xcopri as an important analog (~$315m in MAT IQVIA sales; Yr-3) and we expect any novel anti-seizure med to have a relatively slow and steady launch ramp.

Acronyms: MDD: major depressive disorder; FDA: food & drug administration; Ph: phase; POS: probability of success; FOS: focal onset seizures; CNS: central nervous system.

Investment Rationale

Alkermes

We are Neutral on ALKS on balanced risk/reward. We believe ALKS' product portfolio is relatively mature with minimal opportunities for upside to consensus: 1) '27 Vivitrol LOE limits the likelihood of a material stock re-rating, 2) we expect Lybalvi (key launch) to have an outsized contribution to ALKS growth, but we see limited upside to cons peak sale, 3) on orexin (key pipe), we believe our risk-adj. est. is priced into stock and key de-risking events (own Ph2 data) are likely to occur 2025+.

Amphastar Pharmaceuticals

We rate AMPH Neutral on balanced risk-reward. We believe the bar for Amphastar to re-rate is high at current trading levels. From a risk/reward perspective, downside risks include 1) competitor supply dislocations that have been more recent tailwinds turn into headwinds, 2) pipeline visibility is low. Potential upside could come from the Baqsimi (glucagon rescue) launch which offers more predictable (and visible) growth driver that should help expand company margins in the out-years.

Arcellx, Inc.

We rate Arcellx Buy and like the company based on 1) encouraging Ph1 clinical data for anito-cel (ddBCMA) which looks competitive relative to more advanced players in the relapsed/refractory multiple myeloma CAR-T space, 2) 2024 data readouts are material catalysts with potential to de-risk anito-cel, and 3) upside optionality with SparX approach (we do not currently include SparX programs [early stage] in model).

Arrowhead Pharmaceuticals

We rate ARWR a Buy. We expect ARWR to deliver P&L leverage driven by the rollout of new products that are either wholly owned or partnered (future royalty streams). Our thesis is based on favorable risk/reward in front of several key 2024 catalysts including 1) topline data from Ph3 ARO-APOC3 in FCS in 2Q24 - data could facilitate an NDA leading to ARWR's first approved product, 2) Ph1/2 biomarker data from respiratory assets.

Axsome Therapeutics

We are Neutral-rated on AXSM stock based on our view that there is a balanced risk/reward where Axsome's Auvelity launch as a treatment for MDD is tracking below consensus estimates and we see the company's primary care products are relatively undifferentiated (depression, narcolepsy, migraine). On the flip side, we see these

negatives as being counter-balanced by likely positive Ph3 updates for AXS-12 (narcolepsy) and Auvelity third Alzheimer's agitation readout (1H24).

Bausch Health Cos Inc

We rate BHC an Underperform as we see challenges to value creation in proposed separation of the B&L (eye health) and RemainCo (pharma): 1) RemainCo - key risk is multiple compression as a stand-alone business as the company is highly levered to Xifaxan, which is at risk of earlier than expected (2028) LOE and we see very limited equity value in a >5x levered RemainCo, 2) B&L spin - execution risk

bluebird bio

We rate BLUE Buy. We like the peak sales potential for BLUE's Lyfgenia as a gene therapy for Sickle Cell, a large market for a curative treatment. We believe Lyfgenia's data are competitive with the only other marketed GT for SCD and we believe the company's prior launch of Zynteglo for beta thal has established commercial infrastructure that can be leveraged by Lyfgenia. We see Bluebird as funded to sustain operations to 2025 and we view upcoming quarterly results as key catalysts for the stock

Exelixis

We rate EXEL Buy as we believe the company provides favorable risk/reward on resolution of cabo IP dispute, continued progression of pipeline portfolio, and possible cabo label expansion opportunities. In 2024, we look to data updates on cabo prostate and mid-to-late-stage programs ie zanza and XB002 (TF-ADC).

Harmony Biosciences

We rate HRMY Underperform on lack of high impact catalysts and a challenging path to addressing a '29 Wakix LOE on balanced risk-reward. At this juncture we would have preferred to see the company more active on BD to diversify its product portfolio. Our model is highly sensitive to LOE assumption, assuming Wakix can exceed $1bn in '29+ revenue, though we do not believe it is prudent for investors to assign value to terminal polymorph patent (susceptible to non-infringing alternative polymorphs)

Immunovant, Inc.

We rate IMVT a Buy on upside potential for IMVT's clinical-stage FcRn portfolio. Catalysts include: 1) clinical data for TED and Graves', which are FcRn white spaces, 2) broad applicability in autoimmune diseases that provide further upside beyond crowded markets (MG, CIDP). Keys to the IMVT thesis: 1) broad FcRn commercial opportunity-set, 2) ability of IMVT to differentiate on dosing convenience and potential efficacy differentiation with next-gen drug possessing a favorable therapeutic index.

Intra-Cellular Therapies

We are Buy-rated on ITCI based on peak sales potential for Caplyta in approved and development-stage add-on indications. We believe the commercial opportunity for Caplyta in bipolar depression is substantial given limited approved therapies in this under-penetrated market. We are encouraged by recent MDD competitor launches and we view the 1H24 Ph3 updates for Caplyta in MDD as a meaningful upside opportunity.

Ionis

We rate IONS Buy on favorable stock setup ahead of catalyst-rich path in 2024-1H25. There will be multiple mid-/late-stage clinical readouts that can increase likelihood of success for four assets with $300m-1bn nominal peak revenue estimates (Wainua, donidalorsen, olezarsen, ION582). Approval of Wainua in polyneuropathy with a clean label indicates ION's improved antisense (ASO) platform can mitigate legacy safety issues, effectively validating the safety profile of IONS' broader pipeline.

Jazz Pharmaceuticals
We rate JAZZ a Buy as the company is positioned to shed a long-lived "oxybate overhang" with the recent launch of a Xyrem authorized generic. In our view, strength in '23 numbers bridging to '25 targets is key to improving investor confidence in growth story and we're encouraged to see Epidiolex (seizures) performance uptick. Last, we believe Jazz's emerging pipeline (essential tremor, Zanidatimab programs) is essentially free at current valuation.

Lyra Therapeutics
We are buy rated on LYRA for three reasons: 1) LYR-210, a steroid-eluting implant, has the potential to offer six-months of durable efficacy, 2) steroid incorporated in LYR-210 is a validated treatment for CRS, and 3) LYR-220 offers further expansion into the post-surgical CRS setting, 4) Lyra is attractively valued relative to massive addressable market.

Oculis Holding AG
We rate Oculis Buy on key clinical-stage asset's potential to address unmet need in ophthalmology indications. Upcoming data readouts are expected to further de-risk novel pipeline assets, particularly OCS-01 for diabetic macular edema (full 52-wk data expected in 2H25) and post-ocular surgery related pain and/or inflammation (PC date: July 2024). While there is greater clinical risk associated with earlier stage Ph2 dry eye disease asset OCS-02, we believe there remains an unmet need.

Organon
We rate OGN Underperform for 3 key reasons: 1) OGN's transformation via M&A has been slow to materialize and the company is relatively catalyst-light over next 12-18 mos. 2) while OGN's key growth brand, Nexplanon (long-acting reversible contraceptive) may be able to deliver on management's DD growth target, we don't foresee meaningful upward revisions relative to consensus forecasts for the product. 3) EBITDA trending to low-SD declines annually.

ProKidney Corp
We rate PROK Neutral based on a balanced risk/reward on lack of meaningful de-risking near-term catalysts. REACT's Ph2 bilateral dosing data in 2024 could offer insight on efficacy attributable to bilateral dosing (same dosing as registrational Ph3). However, we believe stock upside is limited by the uncertainty of key de-risking catalyst, REACT Ph3 topline in CKD patients, and 1H24 detailed data of GLP-1 on kidney function, which could begin to inform impact on REACT's market opportunity.

Relay Therapeutics
We rate RLAY Buy on the strength of RLAY's precision oncology pipeline. We like the upside opportunities tied to: 1) RLAY-2608 - a PIK3CAi being developed for metastatic breast cancer represents the largest peak sales opportunity. We will look to key '24 clinical data to de-risk the drug profile, 2) FGFR2i - a selective agent that can dial-out toxicities associated with first-gen agents thereby improving efficacy and mitigating toxicities that hinder the patient's ability to continuously dose.

Roivant
We rate ROIV Neutral on balanced risk/reward. We like IMVT's FcRn franchise and see upside potential from positive development updates, though upside magnitude to ROIV would be reduced by non-controlling interest (ROIV owns about 55% of IMVT). Conversely, ROIV is not yet profitable and continued cash outflow could lead to the Street's discounting ROIV's valuation on cash. We are below consensus on VTAMA sales forecast driven by our more cautious view on the topical psoriasis market opportunity.

Tarsus Pharmaceuticals
We rate TARS Buy on Xdemvy launch as the first FDA approved therapy for demodex blepharitis. We forecast peak sales >$900m given strength of Xdemvy profile, large TAM and lack of competitive alternatives. We view early prescription data as supportive of a favorable launch and look to upcoming quarterly results for validation that the launch uptake is durable and reimbursement is at favorable net pricing. TARS trades at <1x EV/peak sales, and we expect launch validation to drive a share re-rating

Teva Pharmaceuticals
We rate TEVA Buy as we see TEVA moving towards a phase of more predictable top and bottom-line growth. We see '24 financial performance as key for validating: 1) growth of high margin brands is outpacing LOE brands leading to improved margins, 2) stabilizing global gx business: the US segment should benefit from new launches while the ex-US business has been showing low to mid-SD organic growth over last 1-2 years. We also look to pipeline updates: Uzedy launch, olanzapine LAI Ph3, TL1A Ph2 data

Viatris Inc.
We rate VTRS Underperform as VTRS embarks on a slow, multi-year transition phase pivoting to a specialty brand business. While VTRS will have >$2.5bn in divestiture proceeds, VTRS is committed to returning 50% of FCF to shareholders via dividends/buybacks, the size of M&A capacity may be constrained for some time. Some of our concerns near-term are around lack of visibility on pro forma (RemainCo) earnings power (EBITDA), VTRS' ability to make value accretive M&A decisions (limited track record)

Price objective basis & risk

Alkermes (ALKS)
Our $29 PO is based on a blended mix of DCF and 2025E P/E. We believe our DCF is based on reasonable assumptions, including: (1) discount rate of 9%, and (2) risk-adjusted pipeline value for ALKS2680 in lieu of terminal value. Our assumption of 13x '25E EPS is within range of biopharma peers (7-17x) and comparable to 13x where ALKS trades at.

Upside risks: 1) better-than-expected Vivitrol or Aristada sales growth, 2) value accretive divestiture or partnership above our expectation.

Downside risks: 1) worse-than-expected product sales growth, 2) assets divested or partnered at values below our expectation.

Amphastar Pharmaceuticals (AMPH)
Our $63 price objective is based on 12.5x EV/EBITDA multiple based on FY24E EBITDA outlook. We arrive out our 12.5x EV/EBITDA valuation multiple due to a more favorable gross margin and EBITDA margin profile relative to Spec Pharma peers, as well as lower net leverage ratio. As such, the valuation multiple is reflective of that seen with some large-cap pharma companies with comparable growth profiles trading in the 12-13x EV/EBITDA range.

Downside risks: (1) slower than expected commercial uptake of Baqsimi and (2) generics base business erosion

Upside risks: (1) better than expected commercial uptake of Baqsimi, (2) new generic product launches that drive upside to BofA/consensus revenue forecasts

Arcellx, Inc. (ACLX)
Our $65 per share price objective is based on a risk-adjusted, sum-of-the-parts DCF. We assume 1) a discount rate of 10% for a pivotal clinical-stage company, 2) a Probability of Success of 80% for ddBCMA program given that it will soon enter pivotal testing. 3) terminal value with terminal growth rate of 0% to reflect a durable market position for ddBCMA given high capital barriers to competitor entry

Downside risks: 1) ddBCMA trial failure, 2) worse-than-expected ddBCMA clinical data

Upside risks: 1) better-than-expected ddBCMA clinical data and 2) acquisition at a premium.

Arrowhead Pharmaceuticals (ARWR)
Our $37 price objective (PO) is based on a risk-adjusted DCF analysis which assumes 1) risk-adjustment to pipeline programs based on abundance and strength of clinical data with <30% POS assigned to early-stage programs vs >50% POS for mid-to-late stage assets, 2) the biggest value drivers in our DCF valuation are ARO-APOC3 for FCS and sHTG (48%), ARO-AAT (31%) and pipeline programs (59%), 3) we assume 10% discount rate.

Downside risks to our PO: 1) failure of wholly-owned late stage clinical trials, 2) competitor clinical data outperform vs our expectation, 3) failure to partner programs for financing requirements.

Upside potential to our PO: 1) delay to regulatory approval of competitors products, 2) failure of competitors' clinical trials, 3) better-than-expected performance of wholly-owned and/or pipeline assets.

Axsome Therapeutics (AXSM)
Our $80 price objective (PO) is based on a risk-adjusted SOTP analysis. Key assumptions: 1) risk-adjusted sales climb to $1.4bn by 2027E, 2) no terminal value as we forecast sales through the expected drug LOE, 3) 9.5% discount rate. For Sunosi in EDS, we model $335m in peak sales (commercial, fully derisked). Our AXS-05 (Auvelity) peak sales for depression are $1.2bn. For AXS-05 in Alzheimer's agitation, we model $1.7bn in risk-adjusted peak-sales. For migraine, we model $170m in risk-adjusted peak sales for AXS-07. We model AXS-12 narcolepsy risk-adj. peak-sales estimate at $210m. For AXS-14 in fibromyalgia, we model $180m in risk-adj. peak-sales.

Upside risks to our PO: 1) better-than-expected commercial uptake, 2) pipeline validation beyond our assumptions, 3) potential competitive setbacks.

Downside risks to our PO: 1) lower-than-expected commercial uptake of Auvelity in MDD, 2) competitive assets generating significantly better data vs AXSM, 3) potential setbacks on Axsome's execution on pipeline clinical development plan.

Bausch Health Cos Inc (BHC)
Our $6 price objective (PO) is based on a blended valuation, with 50% weighting to eventual spinoff valuation on SOTP basis (11x (peer multiple) of '23E Bausch & Lomb EBITDA), and 50% to blended company multiple that assumes spin delays lead to the market valuing the company as a single entity (6.3x of '23E EBITDA from total company assets based on diversified biopharma peers comp).

Upside risks to our PO: 1) outperformance of new product launches, 2) better-than-expected EBITDA growth, 3) strong performance of Bausch + Lomb segment combined with higher multiples assigned to eye care comps, including Cooper and Alcon

Downside risks to our PO: 1) underperforming revenue from key growth drivers,

including eye care, Xifaxan or new pharma launch products, 2) margin compression - either due to greater than anticipated spend to support new brand launches or faster than expected erosion of diversified brands

bluebird bio (BLUE)
Our $5 PO is based on risk-adjusted discounted cash flow (DCF) analysis. Our DCF assumptions include (1) risk adjustment to programs dependent on their stage and strength of available data, including 100% combined probability of success (POS) for LentiGlobin-TDT, -SCD, and Lenti-D-CALD, (2) no value for earlier-stage programs that lack clinical data, (3) a 10% discount rate and -10% terminal growth value (end of loss of exclusivity period in 2034).

Downside risks to our PO: (1) cancer safety risk for LentiGlobin, (2) LentiGlobin launch underperforming relative to our forecast, either due to limited demand or inability to adequately supply the market, (3) failure to show durable drug response in future data updates involving key assets, (4) competitor data showing efficacy/safety superior to that of company's lead programs, and (5) high cash burn and projected capital expenditure, which may require equity raises.

Upside risks to our PO: (1) clinical data shows superiority relative to competitor programs, and (2) LentiGlobin launch exceeds our expectations.

Exelixis (EXEL)
Our $27 price objective (PO) is based on DCF analysis. We assume the following: 1) Cabometyx US revenue climbs to $2.5bn by '25E as the product maintains a market leading position in 2L RCC and HCC segments, with modest 1L market share for RCC (we model 2L+ mCRPC at 55% likelihood of success adjustment), 2) EXEL's operating margin expands meaningfully from '19 to '25E and beyond, as the company gradually comes out of heavy investment phase on Cabo franchise in out-years (we assume operating margin expands to c56% by '25E), 3) exclusivity for Cabo though January 2030E, 4) 9.5% discount rate and no terminal value.

Downside risks to our PO: 1) clinical trial failure, 2) patent loss or settlement allowing generic entry prior to 2030 expiry of polymorph patent, 3) widening gross-to-net discount for Cabo with increase in Medicare Part D coverage gap.

FibroGen Inc. (FGEN)
Our $0.50 PO is based on risk-adj DCF. We assume: (1) risk-adjustment (% POS) to roxa programs include approx. blended 98% for CKD (ex-US) and 45% for CIA (chemotherapy). (2) 11% discount rate, consistent with our other SMID Biotech coverage, and no terminal value as we forecast through the end of roxa patent life (2033). We risk-adjust roxa cashflows starting in 2026 based on ongoing patent litigation and potential generic entry in 2026-2028 timeframe.

Upside risks to our PO: (1) Roxa CKD wins appeals and LOE to 30+ (2) roxa labeling for cardiovascular risk/cancer is better than our expectations, (3) competitor data readouts show weaker efficacy/safety profile relative to roxa.

Downside risks to our PO: (1) Roxa ex-US launch underperforms vs. our projections due to low demand and/or lower net pricing, (2) competitor data is superior to roxa on efficacy/safety.

Galapagos (GLPG)
Our $44 price objective (PO) is based on a risk-adjusted DCF analysis. We assume the following: (1) Jyseleca forecast for approved indications in the form of royalties, (2) modest pipeline contribution, (3) 9.5% discount rate and 0% terminal growth rate.

Downside risk to our PO: (1) failure of clinical trials, (2) worse-than-expected filgotinib safety profile and/or label.

Upside risks to our PO: (1) acquisition at a premium, (2) higher-than-expected filgotinib sales

Harmony Biosciences (HRMY)
Our $30 price is based on a sum-of-the-parts (SOTP) analysis. Key assumptions: 1) we forecast cash flow for each commercial and near-term pipeline asset through 2032E and discount rate of 9%.

Downside risks are (1) slower-than-expected commercial uptake of Wakix and (2) IP litigation or settlement with generic Wakix manufacturers ahead of LOE.

Upside risks are (1) stronger than expected commercial update of Wakix and (2) FDA decision that we expect could maintain status quo on Wakix marketability in response to a recent Citizen's Petition.

Immunovant, Inc. (IMVT)
Our $51 price objective (PO) is based on a risk-adjusted sum-of-the-parts analysis. 1) batoclimab launches in 2025 and total FcRn nominal sales reach $4.5bn by 2035e, 2) 75% POS for Myasthenia Gravis and Thyroid Eye Disease indications, 2) 65% POS for CIDP, 3) 50% POS for Graves' Disease, 4) no terminal value beyond batoclimab's 2040 LOE and 1402's 2043 LOE, 5) 11% discount rate.

Downside risks to our PO: 1) inability for batoclimab/1401 to adequately mitigate LDL safety signal in clinical trials, 2) less competitive 1402 product profile, and 3) failure to demonstrate efficacy in future clinical trials.

Upside risks to our PO:1) better than expected outcomes in MG, CIDP, and TED clinical trials, 2) clinical success in trials leading to a steeper market ramp and/or penetration.

Intra-Cellular Therapies (ITCI)
Our $82 price objective (PO) is based on a risk-adjusted sum-of-the-parts analysis. 1) Caplyta risk-adjusted sales climb to $2bn by 2027E, before loss-of-exclusivity (LOE) in 2034, 2) no terminal value, 3) operating margin reaching low-60s percentage, 4) 9% discount rate.

Downside risks to our PO: 1) lower-than-expected commercial uptake of Caplyta in schizophrenia, continued COVID disruption keeping a lid on script growth, 2) BPD commercial execution risk, 3) potential setbacks on ITCI's execution on pipeline clinical development plan, e.g. adjunctive MDD, mixed features.

Upside risks to our PO: 1) better-than-expected commercial uptake of Caplyta in schizophrenia, 2) bipolar depression launch significantly above our estimates, 3) further pipeline validation beyond our assumptions, for e.g. Caplyta in adjunctive MDD, mixed features

Ionis (IONS)
Our $62 price objective (PO) is based on a risk-adjusted DCF analysis, in which we assume: (1) risk-adjustment to pipeline programs based on abundance and strength of supportive clinical data, with <30% POS generally assigned to early-stage programs vs. >50% POS for mid-to-late stage assets, (2) the biggest value drivers in our DCF valuation are Wainua, Olezarsen, and Spinraza, (3) we assign marginal value to more speculative, early-stage program, (4) we assume 9.5% discount rate and 0% terminal growth rate.

Downside risks to our PO: 1) key product sales underperform relative to our forecast, 2) failure of key clinical trials, 3) competitor clinical data outperform vs. our expectation.

Upside risks to our PO: 1) delay to regulatory approval of competitors' drug products, 2) failure of competitors' clinical trials, 3) better than expected clinical data readouts

Jazz Pharmaceuticals (JAZZ)
Our $184 price objective (PO) is based on equally blended valuation based on 8x EV/EBITDA of our 2024E EBITDA. Our valuation multiple reflects our confidence in Jazz's ability to navigate patent cliff concerns, and company growth profile. Our EV/EBITDA multiple of 8x compares to the peer group that trades at 6-7x, which we think is appropriate based on JAZZ's growth outlook vs peers. We assume WACC of 9% and terminal growth rate of -3% in our DCF.

Downside risks to our PO are 1) slower-than-expected sales growth from Xywav or Zepzelca launch, 2) slower-than-expected sales growth of Epidiolex, and 3) competitive headwinds to sodium oxybate brand franchise.

Upside risks to our PO are 1) greater-than-expected sales growth from Xywav or Zepzelca launch, 2) less-than-expected generic erosion of Xyrem (eg. due to difficulty setting up a generic REMS), and 3) future business development transactions, which is a core element of the company's strategy.

Lyra Therapeutics (LYRA)
Our $12 price objective (PO) is based on a risk-adjusted sum-of-the-parts NPV model of LYR-210 and LYR-220. Key assumptions: 1) we forecast cash flows through 2037 patent life of LYR-210, 2) 70% likelihood to market for LYR-210 and 70% for LYR-220, 3) LYR-210 and LYR-220 to generate $160m and $30m in 2029E risk-adjusted sales, respectively, 4) discount rate of 12% and no terminal value.

Downside risks to our PO are: (1) failure of LYR-210 or LYR-220 to show desired results in clinical trials, (2) slower-than-expected commercial uptake of LYR-210 or LYR-220, (3) potential dilutive cash raises to commercialize the drug.

Upside risks to our PO are: (1) better-than-expected clinical data and/or commercial uptake of LYR-210 or LYR-220, (2) acquisition at a premium price.

Oculis Holding AG (OCS)
Our $21 price objective is based on sum of the parts (SOTP) analysis. Key assumptions: 1) we forecast cash flow for each near-term pipeline asset through 2035E and 2) discount rate of 9%.

Downside risks are: 1) clinical-stage assets fail to demonstrate stat sig benefit on primary endpoints, 2) slower-than-expected uptake of OCS-01 in post-ocular surgery and/or DME (diabetic macular edema) and OCS-02 in DED (dry eye disease), and 3) higher than expected R&D expenses (impacting cash runway).

Upside drivers are: 1) 2H25 DME Ph3 stage 2 demonstrates that loading dose confers improved efficacy profile, 2) 3Q23 Ph3 data readout of OCS-01 in post-ocular surgery pain/inflammation clears path to est 2025 launch, and 3) positive proof of concept data for OCS-01 Ph2 CME (cystoid macular edema) and OCS-05 Ph2 AON (acute optic neuritis)

Organon (OGN)
Our $12 PO for OGN is based on 5.75x EV/EBITDA multiple on our '24E EBITDA. We believe the multiple is justified vs peers trading at 6-10x given the potential growth

outlook for Nexplanon and biosimilars.

Upside risks to our PO are: (1) higher-than-anticipated Nexplanon peak sales as it expands within the long-acting reversible contraceptive (LARC) category, (2) higher-than-expected operating leverage leading to higher EBITDA margin.

Downside risks to our PO are: (1) reduced uptake of Nexplanon in the LARC category or slow rebound by the LARC category due to C19 other factors and (2) steeper erosion of established brands than expected.

ProKidney Corp (PROK)
Our $2-per-share price objective (PO) is based on a risk-adjusted DCF. We assume (1) a discount rate of 12%, consistent with the rate we use for biotech peers with early clinical data and ongoing late-stage clinical testing, (2) value contribution of $2/share and $0/share for REACT and cash, respectively, (3) a POS of 45% for the REACT program given availability of open label interim clinical proof-of-concept data and currently in Ph3 registrational development, (4) REACT contribution through 2040 - we model a biologic-like product life cycle, although we concede that conventional generics are unlikely and the bigger threat to tail value comes from innovative cell therapy competitor approaches, (5) a terminal value (TV) growth rate of 0%, reflecting long-term value generation of a cell therapy company without the expectation for conventional generics given complex nature of modality.

Downside risks: 1) REACT Ph3 trial failure, 2) REACT fails to demonstrate improved renal function and renal outcomes to justify the high price associated with cell therapy, 3) procedural safety events, or theoretical cell therapy related safety events occurring at unacceptable levels in subsequent data readouts

Upside risks: 1) better-than-expected REACT Ph3 CKD data in early 2025, 2) better-than-expected Ph2 data in the 2023-2024 time frame, 3) potential acquisition at a premium.

Relay Therapeutics (RLAY)
Our PO of $27 is based on a risk-adjusted, SOTP DCF. We assume: 1) a discount rate of 12% for a Ph2 clinical-stage company, 2) likelihood of success (POS) of 5-65% for the FGFR2 program across multiple tumor types, 3) POS of 30% for the PIK3CA program in HER2- breast cancer, 4) 10% POS for platform pipeline, 5) loss of exclusivities of lead programs in the 2040-41E timeframe.

Downside risks: 1) clinical trial failure, 2) FGFR2i or PIK3CAi fails to show differentiated clinical profile vs existing therapies, 3) dilutive equity raise

Upside risks: 1) clinical advancement of FGFR2i or PIK3CAi program, 2) FGFR2i or PIK3CAi finds utility in additional tumor indications, 3) acquisition at a premium

Roivant (ROIV)
Our PO of $12 assumes 1) a discount rate of 11% for hybrid biotech with mid-to-late stage pipeline and a commercial product, 2) POS of 95% for VTAMA atopic dermatitis, 3) risk-adjusted forecast for FcRn franchise, 4) loss of exclusivity of lead programs in 2038E+.

Downside risks to our PO: 1) clinical trial failure or clinical data come in below expectation, 2) product sales underperform our forecast, 3) dilutive capital raise

Upside risks to our PO: 1) clinical data come in above expectation, 2) product sales outperform our forecast, 3) acquisition at a premium

Tarsus Pharmaceuticals (TARS)
Our $42 price objective (PO) is based on a risk-adjusted DCF of TP-03 lead program. Key assumptions: 1) we forecast cash flows through 2038 patent life of TP-03. 2) 100% probability of success for TP-03 and 90% probability of achieving market expansion. 3) TP-03 generates $513m in 2030E risk-adjusted sales, 4) discount rate of 10% and no terminal value.

Downside risks to our PO are (1) failure of TP-03 to show desired results in clinical trials, (2) slower-than-expected commercial uptake of TP-03, (3) potential dilutive cash raises to commercialize the drug.

Upside risks to our PO are (1) better-than-expected clinical data and/or commercial uptake of TP-03, (2) acquisition at a premium price.

Teva Pharmaceuticals (TEVA)
Our $13 price objective (PO) is based on a '24E EV/EBITDA multiple of 8x, which is slightly above the peer group avg of 6.7x reflecting key new product launches following resolution of opioid litigation. Our valuation factors in $4.7bn in contingent legal liabilities related to opioid litigation resolution ($3.2bn) and generic price fixing ($1.5bn). The $3.2bn estimate for present value of opioid resolution cost is based on $4.35bn gross liability, with a 13-year payout.

Upside risks: 1) Ability to execute BD (business development) activity to drive mid-SD revenue growth in '23-27 timeframe, 2) surprise high value new generic product launch.

Downside risks: 1) annual opioid costs may limit BD activity thus hindering TEVA's aspiration of achieving mid-SD revenue growth in '23-27 timeframe, 2) increased price erosion to key spec pharma brands

Vaxcyte Inc (PCVX)
Our $80 price objective (PO) is based on a risk-adjusted DCF analysis. Key assumptions: 1) we forecast cash flows through 2034, with VAX-24 launching in 2026E, 2) we see 55% likelihood to market for VAX-24, 3) we expect VAX-24 to generate $4bn in nominal sales by 2034E, 4) we apply a discount rate of 11.5% and +1% terminal growth rate.
Downside risks to our PO are (1) failure of VAX-24 to show desired results in clinical trials, (2) slower-than-expected commercial uptake, (3) potential dilutive cash raises to develop and commercialize the drug.
Upside risks to our PO are (1) better-than-expected clinical data and/or commercial uptake of VAX-24, (2) acquisition at a premium price.

Viatris Inc. (VTRS)
Our $9 price objective (PO) is based on 5.25x 2024E EV/EBITDA on our pro forma 2024 EBITDA estimate ($4.7bn), which is discounted to the peer group average of 6x. We conservatively incorporate a $1bn contingent liability related to the ongoing civil lawsuit pertaining to generic price fixing, even though we are not aware of any specific wrong-doing pertaining to the legal matter.

Upside risks to our PO: Pipeline opportunities adding sales/EBITDA above estimates, improvement in investor sentiment as new management executes on strategic priorities, higher synergy realization vs anticipated, dividend growth.

Downside risks to our PO: Failure to execute by new management, further decline in Upjohn China business, potential downside to cash flow generation, lackluster execution on business development plans (following the company's recently announced divestitures).

Xenon Pharmaceuticals (XENE)
Our $56 price objective (PO) is based on a risk-adjusted sum-of-the-parts analysis. 1) XEN1101 launches in 2025 and risk-adjusted FOS sales reach est. $1.5bn by 2039, 2) 80% POS for lead FOS indication, 80% POS for PGTCS, and 65% POS for MDD, 4) No terminal value beyond 2040 LOE, 5) 10% discount rate.

Downside risks to our PO: 1) emerging retinal AE in ongoing FOS studies, 2) failure or disappointing results on confirmatory Ph3 FOS study, 3) failure or disappointing results on PGTCS and/or MDD studies.

Upside risks to our PO: 1) better-than-expected results from Ph3 PGTCS study, 2) better-than-expected results from MDD POC studies, 3) clinical success in FOS leading to better adoption and/or steeper market ramp.

Analyst Certification

We, Jason M. Gerberry and Chi M. Fong, hereby certify that the views each of us has expressed in this research report accurately reflect each of our respective personal views about the subject securities and issuers. We also certify that no part of our respective compensation was, is, or will be, directly or indirectly, related to the specific recommendations or view expressed in this research report.

US - Specialty Pharma & Biotechnology Coverage Cluster

Investment rating	Company	BofA Ticker	Bloomberg symbol	Analyst
BUY				
	Arcellx, Inc.	ACLX	ACLX US	Jason M. Gerberry
	Arrowhead Pharmaceuticals	ARWR	ARWR US	Jason M. Gerberry
	bluebird bio	BLUE	BLUE US	Jason M. Gerberry
	Exelixis	EXEL	EXEL US	Jason M. Gerberry
	Immunovant, Inc.	IMVT	IMVT US	Jason M. Gerberry
	Intra-Cellular Therapies	ITCI	ITCI US	Jason M. Gerberry
	Jazz Pharmaceuticals	JAZZ	JAZZ US	Jason M. Gerberry
	Lyra Therapeutics	LYRA	LYRA US	Jason M. Gerberry
	Oculis Holding AG	OCS	OCS US	Jason M. Gerberry
	ProKidney Corp	PROK	PROK US	Jason M. Gerberry
	Relay Therapeutics	RLAY	RLAY US	Jason M. Gerberry
	Tarsus Pharmaceuticals	TARS	TARS US	Jason M. Gerberry
	Teva Pharmaceuticals	TEVA	TEVA US	Jason M. Gerberry
	Vaxcyte Inc	PCVX	PCVX US	Jason M. Gerberry
	Xenon Pharmaceuticals	XENE	XENE US	Jason M. Gerberry
NEUTRAL				
	Alkermes	ALKS	ALKS US	Jason M. Gerberry
	Amphastar Pharmaceuticals	AMPH	AMPH US	Jason M. Gerberry
	Axsome Therapeutics	AXSM	AXSM US	Jason M. Gerberry
	Galapagos	GLPG	GLPG US	Jason M. Gerberry
	Harmony Biosciences	HRMY	HRMY US	Jason M. Gerberry
	Ionis	IONS	IONS US	Jason M. Gerberry
	Roivant	ROIV	ROIV US	Chi M. Fong
UNDERPERFORM				
	Bausch Health Cos Inc	BHC	BHC US	Jason M. Gerberry
	FibroGen Inc.	FGEN	FGEN US	Jason M. Gerberry
	Organon	OGN	OGN US	Jason M. Gerberry
	Viatris Inc.	VTRS	VTRS US	Jason M. Gerberry

Disclosures

Important Disclosures

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.

FUNDAMENTAL EQUITY OPINION KEY: Opinions include a Volatility Risk Rating, an Investment Rating and an Income Rating. VOLATILITY RISK RATINGS, indicators of potential price fluctuation, are: A - Low, B - Medium and C - High. INVESTMENT RATINGS reflect the analyst's assessment of both a stock's absolute total return potential as well as its attractiveness for investment relative to other stocks within its Coverage Cluster (defined below). Our investment ratings are: 1 - Buy stocks are expected to have a total return of at least 10% and are the most attractive stocks in the coverage cluster; 2 - Neutral stocks are expected to remain flat or increase in value and are less attractive than Buy rated stocks and 3 - Underperform stocks are the least attractive stocks in a coverage cluster. An investment rating of 6 (No Rating) indicates that a stock is no longer trading on the basis of fundamentals. Analysts assign investment ratings considering, among other things, the 0-12 month total return expectation for a stock and the firm's guidelines for ratings dispersions (shown in the table below). The current price objective for a stock should be referenced to better understand the total return expectation at any given time. The price objective reflects the analyst's view of the potential price appreciation (depreciation).

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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BofAS or an affiliate was a manager of a public offering of securities of this issuer within the last 12 months: Amphastar Pharmaceut, Oculis, Tarsus Pharma, Vaxcyte, Xenon Pharma.
The issuer is or was, within the last 12 months, an investment banking client of BofAS and/or one or more of its affiliates: Alkermes, Amphastar Pharmaceut, Arcellx, Arrowhead, Exelixis, FibroGen Inc., Intra-Cellular, Jazz Pharmaceuticals, Oculis, Organon, Relay Therapeutics, Tarsus Pharma, Teva Pharmaceuticals, Vaxcyte, Viatris Inc., Xenon Pharma.
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