BofA SECURITIES

US Biopharmaceuticals

Year Ahead 2024: Can the rebound persist for biotech? All signs point to 'yes'

Rating Change

Stars aligning for a sustained SMid Biotech rally in 2024

The NBI closed the year up ~20% (SPX: +15.8% same period) from Oct. 2023 lows, fueled by improving outlook for interest rates, a slew of M&A (BMY/KRTX, ABBV/CERE, ABBV/IMGN), and positive data underscoring continued innovation. The question heading into 2024 is whether this recent momentum is sustainable, and while timing/size of rate cuts is still a point of debate, we see the setup for SMid Biotech as now being markedly improved versus same time last year. We will continue to look for sustained M&A (and remaining dry powder), more predictable stock reactions on catalysts, and early signs of thawing for the biotech funding environment as guideposts to a recovery for the sector.

Beneficiaries and laggards in our coverage

For stocks in our coverage, we continue to like potentially positive launch stories (SWTX, KRYS, HCM) and companies with late-stage clinical readouts (RGNX, MGTX). We would steer away from high-risk binary stocks (DAWN) and companies entering crowded markets with undifferentiated products (NVAX, TGTX).

Top pick: SpringWorks (**SWTX**; Buy, $50 PO) we like for the nirogacestat launch in desmoid tumors and mirdametinib in NF1-PN as an encore which are the focus for many in 2024. Both programs have already stepped through key derisking events, with market opportunity underappreciated and rest of the company's pipeline offering additional upside beyond current valuations if data readouts are positive over next 12-18 months.

Top laggard: Day One Biopharma (**DAWN**; Underperform, $10 PO) is by far the biggest binary in our coverage in 1H24 (PDUFA date for tovorafenib April 30th, 2024). And while no AdCom is generally viewed as positive, we still see multiple areas for potential FDA pushback (RANO-HGG primary, true ORR unclear, single-arm study, growth retardation).

Stocks with potential: We would favor 'value' stocks with big binary phase 3 catalysts over the next 12-18 months, including: **Regenxbio** (**RGNX**; Buy, $35 PO) and **MeiraGTx** (**MGTX**; Buy, $15 PO). We see a positive setup ahead of readouts for both Meira's bota-vec phase 3 in XLRP and Regenx's ABBV-RGX-314 phase 3 in wAMD, with prior phase 1/2 data and large pharma validation increasing PoS, in our view.

Summary of ratings changes

We are upgrading **RevMed (RVMD)** to Buy (from Neutral) and increase our PO to $34 ($31 prior) on growing confidence in the company's RAS(ON) platform heading into additional data updates in 2024e. We lower our rating on **Exscientia (EXAI)** to Neutral (from Buy) with limited opportunities for value inflection over the next 12 months following A2a program discontinuation; lower PO to $9 ($11 prior). We also downgrade to Neutral (from Buy) **Erasca** (**ERAS**, PO to $6 from $11 prior) to reflect narrowed pipeline focus and remaining uncertainty (despite prior derisking data from Novartis) ahead of clinical readouts for naporafenib over the next 6-12 months.

Summary of top sector trends/catalysts and individual company profiles starts on pg 3 >>>

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Exhibit 1: Price objective changes
Summary of updated coverage POs

	Old PO	New PO
RVMD	$31	**$34**
TGTX	$6	**$7**
EXAI	$11	**$9**
MGTX	$18	**$15**
RGNX	$45	**$35**
ERAS	$11	**$6**
NVAX	$5	**$4**
XNCR	$37	**$34**

Source: BofA Global Research

Abbreviations
NBI: Nasdaq Biotech Index
M&A: mergers & acquisitions
SMid: small-/mid-cap
ORR: overall response rate
AdCom: advisory committee
PDUFA: prescription drug user fee act
FDA: Food and Drug Administration
NF1-PN: neurofibromatosis type 1-associated plexiform neurofibromas
RANO-HGG: response assessment in neuro-oncology-high grade glioma
XLRP: x-linked retinitis pigmentosa
wAMD: wet age-related macular degeneration
PoS: probability of success
RAS(ON): active rat sarcoma inhibitor
A2a: adenosine receptor

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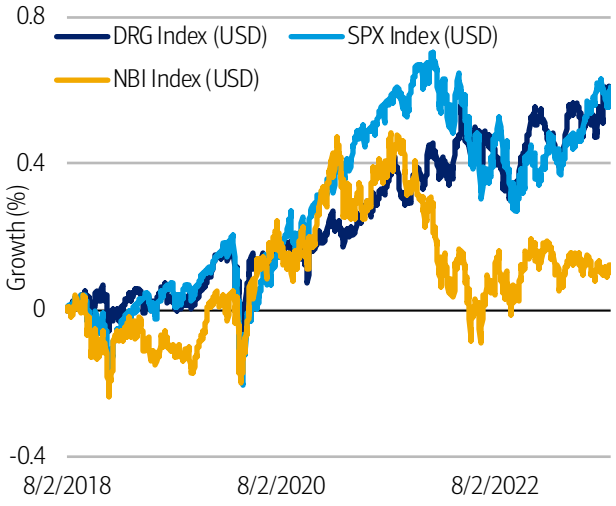
Notable trends heading into 2024

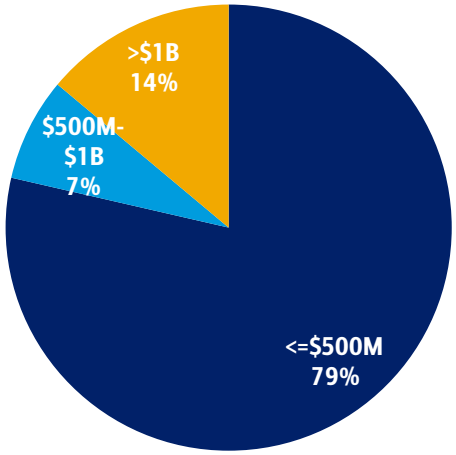
Exhibit 2: Biotech down historically but reversal signals into 2024
Biotech versus the overall market



Source: BofA Research Estimates, Bloomberg

BofA GLOBAL RESEARCH

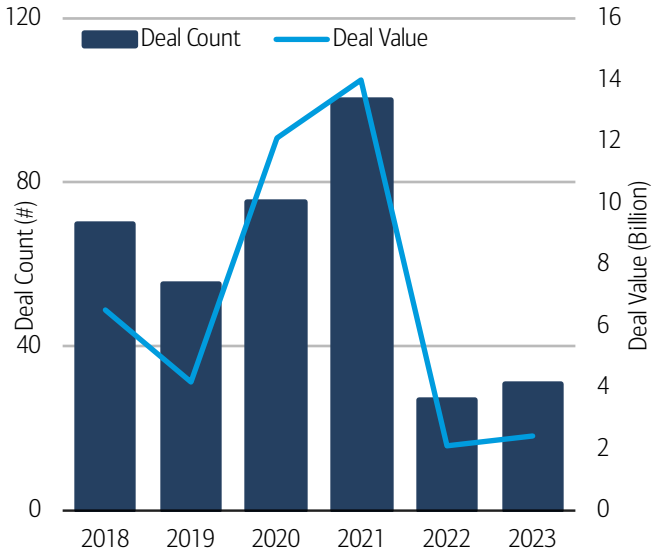
Exhibit 3: Small cap companies dominate in numbers
Breakdown of SMID-biotech industry by market cap



Source: BofA Research Estimates, Bloomberg

BofA GLOBAL RESEARCH

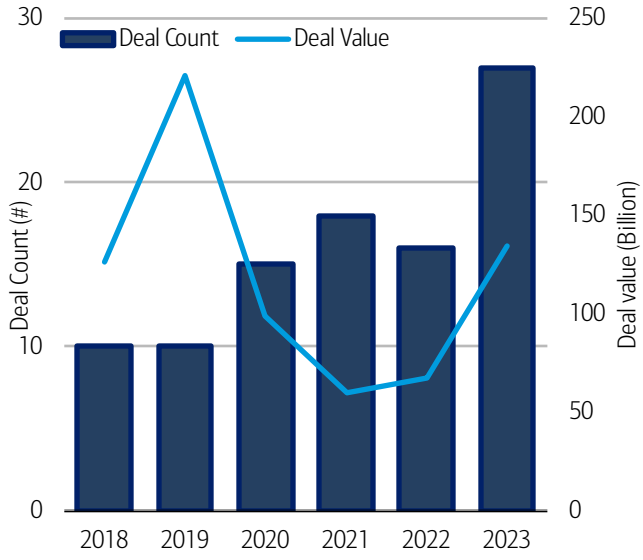
Exhibit 4: 2023 is weak in terms of IPO deals, with 2021 being the peak
Summary of IPO deals last 6 years



Source: BofA Research Estimates, Bloomberg

BofA GLOBAL RESEARCH

Exhibit 5: Overall M&A deal numbers trending up, with value rebound
Summary of M&A deals last six years



Source: BofA Research Estimates, Bloomberg

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2024 Coverage Catalysts

Exhibit 6: Coverage Catalysts
Summary of important catalysts in 2024 for our coverage companies

Company	Ticker	Asset	Indication	Catalyst	Timing	Importance
Day One Biopharmaceuticals	**DAWN**	Tovorafenib	r/r pLGG	Estimated PDUFA	April 30th 2024	HIGH
		Tovorafenib	1L pLGG	FIREFLY-2 pivotal	2024e/2025e	MODERATE
		Pimasertib/Tovo combo	MAPK-altered solid tumors	Combo with tovorafenib data readout	2025e	MODERATE
Erasca	**ERAS**	naporafenib	RAS Q61 solid tumors	SEACRAFT-1 Phase 1b combo signal-seeking efficacy data	2Q24e/4Q24e	HIGH
		naporafenib	NRASm Melanoma	SEACRAFT-2 Phase 3 pivotal study first patient dose	1H24e	MODERATE
		ERAS-007	EC-naïve BRAFm CRC	HERKULES-3 Phase 1b combo dose expansion data	1H24e	MODERATE
		ERAS-801	glioblastoma multiforme	THUNDERBOLT-1 phase 1 monotherapy escalation data	2024e	MODERATE
HUTCHMED	**HCM**	Amdizalisib	3L FL/2L MZL	Phase 2 study readout for potential NDA submission	2024e	HIGH
		Savolitinib/Tagrisso	EGFR TKI ref. Met+NSCLC	SAVANNAH global study readout, NDA aimed for 2025	2024e	LOW
Immatics	**IMTX**	IMA203 (PRAME)	Solid tumors	Program updates	2024e	HIGH
		IMA203CD8 (PRAME) 2nd gen	Solid tumors	Interim date readout	2024e	HIGH
		IMA401 (MAGEA4/8)	Solid tumors	Program updates	2024e	LOW
		IMA402 (PRAME)	Solid tumors	Program updates	2024e	LOW
Krystal Biotech	**KRYS**	Vyjuvek	DEB	2023 full-year earnings update	1Q24e	HIGH
		KB407	Cystic Fibrosis	Program updates	2024e	MODERATE
		KB301	Wrinkling/Acne (collagen type III)	Initial phase 1 data	2024e	LOW
MeiraGTx	**MGTX**	botaretigene sparoparvovec (AAV-RPGR)	XLRP	Phase 3 Lumeos study readout	2024e	HIGH
		AAV-AQP1	xerostomia	Phase 3 start	2024e	MODERATE
		AAV-GAD	Parkinson's Disease	IND opening study readout	2024e	MODERATE
		Riboswitch platform	Salivary gland	First phase 1 gene regulation study readout	2024e	MODERATE
		AAV-RPE65	RPE65-associated retinal dystrophy	Phase 3 pivotal study readout	2024e	MODERATE
		AAV-CNGA3/B3	achromatopsia	Late-stage study readout	2024e	MODERATE
Novavax	**NVAX**	Nuvaxovid	COVID-19	2023 full-year earnings	1Q24e	MODERATE
Regenxbio	**RGNX**	RGX-202	DMD	Data update	2024e	HIGH
		RGX-121	MPS II	Pivotal phase 3 readout to support BLA filing in 2024/25	2024e	MODERATE
		RGX-314	wAMD	Phase 3 study enrollment (vs Lucentis and Eylea)	2025e	MODERATE
		RGX-314	Diabetic retinopathy	Phase 2 suprachoroidal further readout	2025e	MODERATE
Revolution Medicine	**RVMD**	RMC-6236	Multi	Phase 1/1b monotherapy interim update	2024e	HIGH
		RMC-6291	G12C	Phase 1/1b monotherapy interim update	2024e	HIGH
		RMC-4630	SHP2	Global phase 2 topline update	2024e	LOW
		RMC-5552	mTORC1-4EBP1	Additional evidence of monotherapy activity	2024e	MODERATE
SpringWorks Therapeutics	**SWTX**	Mirdametinib	NF1-PN	NDA submission	2024e	HIGH
		Nirogacestat/Blenrep	Multiple Myeloma	Data readout for Blenrep combo	2024e	HIGH
TG Therapeutics	**TGTX**	Briumvi	RMS	2023 Full-year earnings update	1Q24e	HIGH
Y-mAbs Therapeutics	**YMAB**	GD2-SADA	Solid tumors	Interim phase 1 data	2024e	MODERATE
		GD2-CD38 Bispecific	Liquid tumors	Early phase 1 data	2024e	MODERATE
		Danyelza	osteosarcoma	Phase 2 data and pivotal phase 3 study start	2H24e	LOW
		Danyelza	1L Neuroblastoma	Phase 2 interim readout	1H24e	LOW
		Naxitamab	NB	BCC study phase 2 readout	2024e	LOW

Source: BofA Global Research

Day One Biopharmaceuticals

DAWN US – Rating: UNDERPERFORM (C-3-9) | PO: 10.00 USD | Price: 14.32 USD

What we expect in 2024: regulatory risks to continue

Since D/T combo approval hinted that RANO-LGG is the preferred endpoint for the FDA in pLGG (see our thoughts on how it affects DAWN), we see the company's presentation of data showing lower ORR (RANO-LGG: 49%; RANO-HGG: 67%), and significant delta in tumor reduction >50% (RANO-LGG: 26%, 0% CR; RANO-HGG: 61%, with 6% CR), as adding an area for potential regulatory pushback for tovorafenib (see other overhangs from our downgrade). Company highlighted that FDA commentary so far has been positive, and the agency will be taking a holistic look at both HGG/LGG endpoints. That said, ORR under the additional RANO-LGG exploratory analysis might still be an area of FDA pushback in our view even with NDA filing acceptance. Therefore, 2024 is very much a year of binary outcome for the biotech and we outline possible scenarios including **1)** Positive: No AdCom straight approval, **2)** Negative: AdCom and subsequent CRL. Maintain Underperform and $10 PO.

Key debate: AdCom could still happen, CRL not ruled out

While it is generally expected that the FDA will announce the presence of an AdCom with NDA acceptance, we note that it is not uncommon for the agency to announce AdCom meeting later than that date, especially with the FDA specific guidance on AdCom stating that "FDA AdCom can be decided at any stage of a review process, and typically not utilized when the data clearly support or clearly does not support the safety and effectiveness of the therapy". There are also recent examples of delayed FDA scheduling of AdCom including Sarepta's SRP-9001, which received BLA acceptance on Nov. 28th, 2022, but was not notified of an AdCom until April 10th of 2023. Moreover, it is also not unheard of for FDA to give straight CRL with no AdCom, with Phathom Pharmaceuticals' filing of NDA of Vonoprazan accepted in May 2022, no AdCom, but CRL'ed in Jan. 2023 (we do note that Vonoprazan review was standard not accelerated). Therefore, we still see possibility of **1)** FDA later announcing the hosting of an AdCom, **2)** possibility of CRL still existing. Either way, we think it is still too early to say.

Notable 2024 clinical catalysts

2024 will not be a big year for DAWN in terms of clinical catalysts, rather, majority of investor focus will be centered upon April 30th, 2024 PDUFA date for tovorafenib. We do not expect readouts from 1L pLGG trial nor pima/tovo combo until next year, although cannot completely discount an interim look at the data in 2024. Therefore, the mission for the company in 2024 is clear: tovorafenib PDUFA. We preempt the possibility of a 3-month delay for the review process (as apparent given recent trends exhibited by the FDA), hence we expect a verdict will be granted in April-July of this year.

Valuation / P&L thoughts heading into 2024

Our $10/share price objective is based on a probability adjusted NPV for tovorafenib in r/r pLGG ($2/sh), tovorafenib for 1L pLGG ($1/sh), tovorafenib for RAF-driven solid tumors ($1/sh), pimasertib/tovorafenib combo for RAF-driven solid tumors ($1/sh), and cash ($5/sh). We apply a WACC of 10-12% and 1% (tovorafenib) to 3% (pima/tovo combo) terminal growth rate. Tovorafenib in the relapsed/refractory setting, if approved, will generate ~$833M peak revenue in 2031 in US/EU (+$30M cons), but anything other than an approval will likely delay revenue generated by at least 1-2 years and lowering peak revenue meaningfully (our sensitivity analysis showed decrease in peak sales by as much as 31%, see our sensitivity analysis here).

Tovo: Tovorafenib

r/r: Relapsing

pLGG: Pediatric low-grade glioma

NBI: Nasdaq biotech index

NDA: New drug application

ORR: Overall response rate

AdCom: Advisory committee

FDA: Food and drug administration

Pima: Pimasertib

1L: Front line

PFS: Progression free survival

OS: Overall survival

PoS: Likelihood of success

ODAC: Oncologic drug advisory committee

BRAF: v-raf murine sarcoma viral oncogene homolog B1

Erasca

ERAS US – Rating: NEUTRAL (C-2-9) | PO: 6.00 USD | Price: 2.16 USD

What we expect in 2024: Naporafenib now the focal point

Naporafenib (acquired from Novartis, see our thoughts on the asset acquisition) has shifted the balance of Erasca's pipeline to late-stage development, with previous data from 500+ patients already demonstrating safety and preliminary efficacy both as monotherapy and combination setting. SEACRAFT-1 phase 2 is enrolling RAS Q61X solid tumors (initial data 2Q-4Q24e) and SEACRAFT-2 phase 3 will begin dosing NRASm melanoma patients in 1H24e. And while we like the napo acquisition as it accelerates path to a pipeline approval by 2-3 years, lack of meaningful responses from the rest of the pipeline ('007, '601, etc.) continues to be an overhang. Given the complexity of Erasca's approach to shutting down the RAS/MAPK pathway with true resolution on clinical activity unlikely in the next 12 mos, we remain reserved heading into the next slew of data updates. We lower our rating to Neutral (from Buy) and adjust our PO $6 (from $11) to reflect a narrowed pipeline focus and remaining uncertainty (despite prior derisking data from Novartis) heading into clinical readouts for naporafenib over the next 6-12 months.

Key debates: what changes the narrative for Erasca?

Data readouts from ASCO and AACR (see our thoughts on readout from ASCO, AACR), and a few discontinued programs (KRAS G12C, SHP2, ERK combos) contributed to share weakness in 2023 (-52%; NBI: +4.7%). ERAS-007/EC combo demonstrated a 50% (3/6) ORR in EC-naïve patients (26.8% ORR for BEC triplet in phase 3 BEACON trial, 19.5% ORR for EC doublet), which is strong but small and makes data less actionable for investors. '601 (SHP2) combo with cetuximab readout from AACR also showed limited responses, despite some early monotherapy activity. And while these data warrant further clinical investigation, we see meaningful responses in the clinic across the pipeline (particularly for napo) as needed to improve investor sentiment in 2024. Looking to SEACRAFT-1 readout next year (RAS Q61X solid tumors), we see maintained efficacy from the previously reported 47% ORR (80% DCR) from the combo and 5 mo PFS (~1.5 mo seen with SoC) as the bars to hit.

Notable 2024 clinical catalysts

Following recent strategic prioritization of programs, we see focus shifting towards combos, ERAS-801 in GBM, and naporafenib with multiple readouts expected in 2024e including **1)** SEACRAFT-1: phase 1b trial for naporafenib plus trametinib initial combo data between 2Q24e and 4Q24e, **2)** HERKULES-3 phase 1b trial for ERAS-007 plus EC combo expansion data expected between 2H23e and 1H24e, **3)** THUNDERBOLT-1 phase 1 trial for ERAS-801 monotherapy dose escalation data expected in 1H24e and dose expansion data in 2H24e. Together, we expect a good flow of data catalysts over the next 12-18 months, the totality of which carry risk but could help reverse momentum for shares.

Valuation / P&L thoughts heading into 2024

Our updated $6/sh price objective is based on a probability adjusted NPV of naporafenib ($2/sh), ERAS-007 ($1/sh), ERAS-601 ($0/sh), ERAS-801 ($1/sh), the discovery pipeline ($0/sh), and cash ($2/sh). Trimming of the pipeline in 2H23 extends the company's cash runway from 2H24 to 1H26, which should cover potential points of value inflection from naporafenib, ERAS-801, and ERAS-007. With $343.6M cash and equivalents on hand at the end of 3Q23, we see the company's current market capitalization of $326.3M as essentially trading in-line with cash, giving little value to naporafenib or the rest of Erasca's pipeline. And while the in-licensing of naporafenib opens potentially lucrative new markets (~3.5M patients WW) and more synergistic potential leveraging multiple combo strategies, at this point we see Erasca as more of a "show me story", with the company's approach to shutting down the RAS/MAPK pathway still requiring further validation in the clinic.

Napo/tram: naporafenib/trametinib combo

RAF: Rapidly accelerated fibrosarcoma

ORR: Overall response rate

PFS: Progression free survival

SOC: Standard of care

RAS: Kirsten rat sarcoma

Q61X: Mutation on codon 61

ERK: extracellular signal-regulated kinase

MAPK: Mitogen-activated protein kinase

DOR: Duration of response

SHP2: tyrosine phosphatase-2

ASCO: American Society of Clinical Oncology

AACR: American Association for Cancer Research

Exscientia

EXAI US – Rating: NEUTRAL (C-2-9) | PO: 9.00 USD | Price: 6.55 USD

What we expect in 2024: AI validation still long way away

While we see onset of ChatGPT introducing attention to the broader AI space, AI in healthcare in our view has still a longer way to go for it to become 'mainstream'. In our view, computing power and algorithms are not clear enough differentiators for AI companies especially in drug discovery, with data uniqueness being the ultimate decider. As our recent KOL checks have concluded, data quality is especially important for training AI models; lackluster quality could turn an AI model into a "garbage regurgitator". Many companies are on the hunt to mine the most unique data they can, with future ways of self-collection an especially attractive feature for AI companies. With EXAI's upcoming readouts still on the earlier side, we do not expect validation of the company's platform or approach (the true point for value inflection, in our view) to come in the next 12 months; we downgrade our rating to Neutral (from Buy) and lower PO to $9 ($11 prior) to reflect potentially elongated timelines.

CDK7 and LSD1 program development set to accelerate

While deprioritization of the A2a program (formally the company's lead asset) could be viewed as a negative, we see path to clinical validation of Exscientia's platform as not meaningfully affected, however true clinical validation from the pipeline is still likely 1-2 years away. Furthermore, the evolving knowledge of the A2a target creates a tougher setup, with a next-gen A2a asset under development potentially solving PK issues for future partnership. We therefore see investment in other areas of the pipeline as more productive in 2024. The phase 1/2 for GTAEXS617 (CDK7) continues to enroll patients, with initial clinical readouts likely in 2024/2025e helping to validate the company's AI-driven clinical trial design capabilities, if positive. EXS74539 (LSD1) is also advancing towards the clinic (prioritizing SCLC and AML) with an IND filing (study in healthy volunteers) expected in 1Q24e.

Notable 2024 clinical catalysts

Multiple preclinical programs remain on track to meet the company's goal of introducing four clinical assets by 2024e, including: **1)** AACR highlighting two programs, '546 and EXS4539, **2)** newly announced wholly-owned precision designed molecules, '539 (LSD1 inhibitor) and EXS73565 (MALT1 inhibitor), **3)** DSP-2342, third compound from the Sumitomo pharma collab, will enter phase 1 clinical trials, **4)** data of first-in-human study of EXS4318 in 2024e. And while the company has not provided concrete guidance on timing of next clinical updates, we continue to see near-term data as likely to be more incremental in nature, with most investors focused on broader platform validation, which we see as likely having a longer time horizon for value inflection.

Valuation / P&L thoughts heading into 2024

Our $9 PO is based on a probability-adjusted net present value (NPV) of Exscientia's lead pipeline assets, as well as value assigned to the early-stage assets, the Bristol Myers Squibb collaboration, and the underlying technology platform itself. We apply a 15% weighted-average cost of capital (WACC, we project revenues out through 2040), in line with other biotech companies of similar size and stage of clinical development. While we do acknowledge that valuing the AI-driven platform is difficult, we currently assess ~$5/sh value for EXAI's AI-driven platform by triangulating opportunity cost, data storage cost as well as valuation based on deal premiums. Clinical-staged pipeline products, namely the CDK7 asset, in our view account for much of the valuation (~41%) but could increase meaningfully if 2024 readouts are fruitful enough to be actionable. Moreover, we see possibility of pipeline validation ultimately raising the ceiling for platform valuation. That said, the time horizon could be much longer than investors expect.

ROI: return on investment

ESMO: European Society for Medical Oncology

SCLC: small cell lung cancer

AML: acute myeloid leukemia

CDK7: cyclin dependent kinase 7

A2a: A2A adenosine receptor

LSD1: Lysine specific demethylase 1

AACR: American Association of Cancer Research

KOL: Key opinion leader

HUTCHMED

HCM US – Rating: BUY (C-1-9) | PO: 29.00 USD | Price: 17.23 USD

What we expect in 2024: the Fruzaqla watch is on

In our view, Fruzaqla can become a "monster drug" and 2024 is the year to prove it. With US representing an immediate ~27k+ addressable patient and ~$300M peak revenue opportunity for HUTCHMED and Takeda, with additional upside from label expansions (GC, NSCLC) and approvals in EU and Japan (filings currently under review), combined with Takeda's already-existing expertise in oncology drug commercialization, we see little hurdles ahead for Fruzaqla. US approval triggered a $35M milestone to HUTCHMED ($1.13B total milestones under the deal, including $400M upfront earlier this year). The company is also eligible to receive royalties on net ex-China product sales, which we estimate could be close to 20% based on transactions for other assets at a similar stage of development (see our thoughts on the deal). We also expect a WAC price in the range of $10-12k per month would put it roughly in-line with competing oral therapies approved for mCRC. That said, early quarters of 2024 are especially important to gauge launch trajectory, which we will continue to keep a focus on. Maintain Buy and $29 PO.

Key debate: wave 2 assets on the move, can drive shares

With wave 1 assets (fruquintinib, surufatnib, savolitinib) ramping well into commercialization and especially with fruquintinib as potentially the company's first asset approved in the US market, we see wave 1 assets as gradually shifting to a more "focus on topline" story with wave 2 assets, namely amdizalisib, sovleplenib, coming in to fill the role as the "clinical drivers". In our view, we see HUTCHMED's pipeline as well-bolstered to present investors with not only near-term commercial presence but also long-term innovation upside, not to mention wave 3 assets (BTKi, IDH1/2i etc. see our AACR takeaways), which we currently do not account for in our model, but in our view extends a strong momentum even into 2029+. We also note that sovleplenib in ITP could be an asset to watch in 2024 for the company given the small yet lucrative opportunity it represents. ITP, while not often regarded as having a large end-market, can still represent sizeable topline contribution in our view. Based on the incidence of primary ITP in adults, 3.3/100k adults per year with a prevalence of 9.5 per 100k adults, we estimate approximately 110k patients living with primary ITP in China, in addition to 56k patients in the US/EU (145k with chronic ITP ex-China), our model projects peak market sales of ~$978M for sovleplenib in ITP by 2033 in China (we current assess a 30% PoS for sovleplenib in ITP), with potential label expansion into NHL adding an additional ~$328M in peak sales by 2034 (China/US/EU). With consensus yet to factor in sales from the asset, we see the market underappreciating the ITP opportunity which in our view can bring in sizeable value contribution.

Notable 2024 clinical catalysts

Wave 2 assets account for the most notable clinical catalysts for HUTCHMED in 2024 include **1)** amdizalisib readout in 3L FL and 2L MZL, **2)** potential NDA filing in China for Sovleplenib (company has not provided concrete updates/timelines). That said, we expect 2024 focus for the company to be shifting away from its clinical pipeline and to global commercialization of Fruzaqla. While we still believe that HUTCHMED's robust pipeline will add long-term value to the company, near-term needle-moving activities will rely heavily on Fruzaqla launch.

Valuation / P&L thoughts heading into 2024

Our PO of $29 is derived from a probability-adjusted net present value (NPV) analysis, including $7/share for savolitinib, $10/share for Fruzaqla, $4/share for surufatinib, $1/share for amdizalisib, $1/share for sovleplenib, -$2/share for other pipeline assets, $3/share for the commercial platform and $5/share for net cash. We see possibility of increased value contribution from Fruzaqla especially with EU approval imminently expected in 2024 by our estimates.

GC: Gastric cancer

mCRC: metastatic Colorectal cancer

NSCLC: non-small cell lung cancer

WAC: wholesale acquisition cost

BTK1: Bruton tyrosine kinase

IDH1/2: isocitrate dehydrogenases types 1 and 2

AACR: American Association of Cancer Research

ITP: immune thrombocytopenic purpura

Immatics

IMTX US – Rating: BUY (C-1-9) | PO: 16.00 USD | Price: 10.72 USD

What we expect in 2024: data updates throughout 2024

While IMA203 update has been mostly positive, including **1)** 33% (n=1/3) ORR in newly efficacy-evaluable melanoma patients at RP2D since last update, **2)** broad range of duration on therapy (2.2-14.7 mo), and **3)** unclear additional benefit from the early data for IMA203CD8 GEN2 on efficacy and particularly tolerability. We see the data leaving questions unanswered for investors, which will hopefully come into better resolution in 2024. As outlined in our data preview (see our thoughts on the data readout), we expect IMTX shares to gain momentum if IMA203 is able to hold the same ~50% ORR in the larger phase 2 study, while maintaining similar safety profile. Hence our thoughts on a good "bar" would be **1)** >50% ORR, **2)** no ICANS, low-grade CRS acceptable, **3)** >9mo DOR, which to date looks to be upheld from IMA203's clinical profile. Maintain Buy and $16 PO ahead of additional clinical data readouts across the pipeline.

Melanoma cohort efficacy promising, ICANs to be watched

Safety profile for '203 in melanoma continues to uphold previous standards (melanoma the first indication for the PRAME asset to go after), including **1)** mild-moderate CRS for all 16 patients, **2)** no dose-dependent increase of CRS, **3)** no DLTs, and no IMA203-related deaths observed. That said, we do note that there was one non-serious, mild (Gr 1) ICANS. As for efficacy, 50% cORR (6/12) in our view meets the bar previously set by our estimates (min 2.2+ months, max 14.7+ months) at a median follow-up (mFU) of 14.4 months. While median DOR not reached, we see patients responding as long as 14mo+ as adding incremental confidence to the efficacy profile. That said, we do note that ORR from November is marginally lower compared to May interim data readout (cORR 67% (6/9), ORR 64% (7/11)), but still competitive versus other standard-of-care in 2L+ melanoma. In summary, while efficacy remains to be '203's strong suit, we expect more investor attention to the safety aspect (especially with comp showing no ICANS at all, i.e. IMC-F106C from Immunocore) which '203 must prove in 2024 to address lingering concerns.

Notable 2024 clinical catalysts

From our last conversation with management, we see a clear catalyst path ahead with updates expected across pipeline programs throughout 2024 including: **1)** IMA203 GEN1 update on clinical development, targeting registration-enabling phase 2 trial for ACTengine for melanoma patients (company will likely update on the plan going forward in 1Q24e), **2)** IMA203CD8 GEN2 interim data update with longer follow-up planned, **3)** TCER® IMA401 (MAGEA4/8) first clinical data update from dose escalation in ongoing phase 1 trial planned, **4)** TCER® IMA402 (PRAME) first clinical data update from dose escalation in ongoing phase 1/2 trial planned (initial focus indications: Ovarian cancer, uterine cancer, lung cancer, melanoma and others). While the company has not guided to specific timeframes as to when the data updates will happen, we expect most of the readouts will likely happen over the course of 2024.

Valuation / P&L thoughts heading into 2024

Our $16/share price objective is based on a probability adjusted NPV of lead TCR-T ACTengine programs including IMA402/401Bispecifics ($4/share), IMA203 ($7/share) and cash and equivalents which contributes $5/share. We apply a WACC of 12% given novel nature of Immatics' platform and no terminal value (we project out revenues through 2035). While we see IMA203 as taking the charge in terms of value-add, we see 2024 as the first year investors will get initial look at the PRAME bispecifics (IMA401/402) which can provide additional confidence and drive shares in 2024 if readouts are both meaningful and positive.

PR: partial response

cPR: confirmed partial response

ORR: overall responses rate

cORR: confirmed overall responses rate

CRS: cytokine release syndrome

ICANS: immune effector cell-associated neurotoxicity syndrome

PRAME: preferentially expressed antigen in melanoma

TCR: t-cell receptor

DOR/mDOR: duration of response/median duration of response

KOL: Key opinion leader

DLT: dose limiting toxicity

mFU: median follow-up

CD8: cluster of differentiate 8

SD: stable disease

Krystal Biotech

KRYS US – Rating: BUY (C-1-9) | PO: 140.00 USD | Price: 120.13 USD

What we expect in 2024: Early Vyjuvek launch in focus

KRYS shares outperformed in 2023 (+56.6%; NBI: +4.7%) following approval of their lead gene therapy asset Vyjuvek (in-line with our Buy thesis), which represents the first drug approval for patients DEB. With a broad label in hand (see our thoughts post-approval) and a clear go-to-market strategy, the onus is now Krystal to deliver on the launch in 2024 while pushing forward the rest of their internal gene therapy pipeline. And while we expect the majority of investor focus will remain on the trajectory of the launch (at least in the 1H24), we do see room for shares to trade higher if early studies in CF and oncology yield positive results over the next 12-18 months. We will continue to look at new start forms and conversion of patients to active therapy as leading indicators for future sales momentum in 4Q23/1Q24, although we expect the company should be in good shape to meet our sales expectations near-term ($30.3M BofA in 4Q; +$0.7M cons). Maintain Buy and $140 PO.

Key Debate: Can Krystal build out the DEB market

Given a narrow sales miss in 3Q23 ($8.6M actual vs $9.3M cons), our recent inbounds have entirely revolved around expectations for 4Q and Vyjuvek sales guidance heading into 2024. Together, we see 284 new patients start forms from 136 unique prescribers end of 3Q as a strong start, with the company suggesting 4Q start forms should match, if not exceed 3Q numbers. Further, the 85% conversion rate looks set to increase over the next 6-9 months (20% of identified patient pool penetrated to date) given positive coverage determinations from all major commercial national health plans, which in our view can accelerate uptake in 2024. And while peak sales for Vyjuvek are likely the biggest swing factor for valuation, directional commentary from the company on patient receptivity could also begin to help inform timing/ magnitude of peak sales over the next quarter or two, in our view.

Notable 2024 clinical catalysts

Key focus continues to be Vyjuvek commercial execution, with the stock likely to move around quarterly earnings over the course of 2024. Beyond Vyjuvek, we look to initial phase 1 data for KB407 in cystic fibrosis (cohort 1 enrollment completed, cohort 2 enrollment set to begin imminently), as well as cohort 3 from the phase 1 study KB301 for lateral canthal lines at rest (see our thoughts on the latest aesthetics update) in 1H24e. The addition of KB707 (HSV-based vector delivery of IL-2 and IL-12) to the Krystal story focusing in two tissue areas, the skin and the lungs, both of which, in our view leverages the company's previous clinical experience and expands the broader potential of HSV-1 platform. Key catalysts to watch include: **1)** first-in-human intratumoral KB707 data in 2024, **2)** first patient dosed with inhaled KB707 in 1H24e.

Valuation / P&L thoughts heading into 2024

With first Vyjuvek commercial sale occurring at the end of August (284 new starts are from 3 months in 3Q23), we still see room for Krystal to beat our expectations for FY23 (we project 237 patients on therapy by end of 2023; BofA: $38.9M 2023 sales, cons: $38.2M). Assuming a roughly 4-6 week time for new start forms to convert to paid drug and an 85% conversion rate, the majority of new starts reported in 3Q should be given at least one commercial dose of Vyjuvek by the end of the year, by our estimates. At the current rate, ~$35-40M for 2023 is not out of reach (284*500k pricing*85% G/N*90% compliance*0.3 median duration of therapy). Our $140/share price objective is based on a probability adjusted NPV for rare dermatology ($102/sh), respiratory including CF and AATD ($8/sh), aesthetics through the Jeune subsidiary ($6/sh), the discovery pipeline ($3/sh), and cash ($21/sh).

DEB: dystrophic epidermolysis bullosa

HSV: herpes simplex virus

IL-2/12: interleukin 2/12

G/N: gross-to-net

CF: cystic fibrosis

AATD: alpha-1 antitrypsin deficiency

MeiraGTx

MGTX US – Rating: BUY (C-1-9) | PO: 15.00 USD | Price: 6.77 USD

What we expect in 2024: Janssen deal adds confidence

2024 is shaping up to be an important year for Meira, which should include updates from the XLRP program recently acquired by Janssen (phase 3 Lumeos study enrollment target surpassed as of Aug. 2023), phase 2 xerostomia study progress (now enrolling) and interim data, and additional partnerships for riboswitch platform expected. And while we expect many investors will likely continue to focus on bota-vec for XLRP as the main value driver for shares, we see the recent Sanofi equity transaction (at a premium) as a nod to the riboswitch platform which is a growing part of the narrative (see our thoughts on the deal). The all-stock transaction gives Sanofi the right of first negotiation for use of the company's riboswitch gene regulation technology for certain I&I and CNS targets, as well as for GLP-1 and other gut peptides for metabolic disease, and for the company's Phase 2 xerostomia program. Overall, we see recent deals as simplifying and validating the MeiraGTx story heading into a busy 2024 for the company. We reiterate our Buy rating given our positive view for upcoming data updates and lower our PO to $15 (from $18 prior) based on dilutive effects long-term on riboswitch platform value following deal with Sanofi.

Key debate: Janssen XLRP acquisition drives stock rerating

With the IND for bota-vec now fully transferred to partner Janssen, the phase 3 Lumeos study remains on track with a topline readout (and subsequent BLA submission) planned in 2024. The study completed enrollment in 2Q23 with a target enrollment of ~100 patients according to clinicaltrials.gov. Full data presented from the company's phase 1/2 study of AAV-RPGR at AAO 2022 (and humoral immune response data at AVRO 2023) in our view adds confidence heading into phase 3 readout on both static perimetry and visual acuity, as well as functional assays including the maze test (see our takes on the latest XLRP data). As Meira still stands to gain an additional $285M from Janssen upon first commercial sale of bota-vec in the US and EU, we continue to view the phase 3 readout in 2H24e as a value driver for shares (although we expect many view the timing of the deal as derisking ultimate success for the study).

Notable 2024 clinical catalysts

By far the biggest focus/value driver for Meira in 2024 will be readout of the phase 3 Lumeos study. Beyond XLRP, we expect additional data updates including: AAV-GAD Parkinson's data from the bridging study which is likely more incremental and some updates from the riboswitch platform either internal or Sanofi partnered which could help expand this arm of the story but is likely to be early data. Phase 2 xerostomia study progress (now enrolling) and interim data (see our thoughts on the phase 1 data), as well as additional partnerships are also expected. We continue to like the setup for shares heading into potential points of inflection this ayear.

Valuation / P&L thoughts heading into 2024

With roughly $1/sh in cash as of the end of 3Q23 (not including Janssen payment), we see the current share price of $6.77 as only giving partial value to riboswitch platform and XLRP economics ($4/sh in our model) and xerostomia ($5/sh in our model with a 22% probability of success), with little-to-no value given to the rest of the pipeline (Parkinson's, ALS, riboswitch) or Meira's established in-house vertically-integrated and scalable cGMP manufacturing capabilities (despite recent Forge acquisition as a positive lateral). Furthermore, the $7.50/sh purchase from Sanofi still represents a sizeable premium to current share price, with the deal underscoring riboswitch's growing contribution to the narrative and maintaining robust economics for Meira across the pipeline. Further, newly announced Janssen deal pulls forward XLRP economics by about 3-4 years, with Meira still eligible to receive manufacturing-based payments to support the launch, which should provide a topline bump in the medium-term.

XLRP: X-linked retinitis pigmentosa

AAV: Adeno-associated virus

IND: Investigational new drug application

Xerostomia: severe dry mouth

AAO: American Academy of Ophthalmology

AVRO: Association for Research in Vision and Ophthalmology

BLA: biologics license application

cGMP: current good manufacturing practice

I&I: immunology and inflammation

CNS: central nervous system

ALS: amyotrophic lateral sclerosis

Novavax

NVAX US – Rating: UNDERPERFORM (C-3-9) | PO: 4.00 USD | Price: 5.16 USD

What we expect in 2024: we remain negative on uptake

With FDA authorizations and CDC recommendations in hand, commercial rollout for Novavax's vaccine is well underway. Earlier in Sept. 2023, the company announced doses of its updated vaccine had been delivered to the US and are ready to be made widely available in pharmacies across the country. And while we expect small initial orders to be placed to stock the vaccine, which should be reflected in 4Q revenues, subsequent orders through the remainder of the 2023-2024 COVID-19 season will likely be demand-driven. We continue to monitor sales trends as the company is still "going concern" and reiterate our Underperform rating and lower our PO to $4 ($5 prior) to reflect decreasing window for the company to rebound in a shrinking C-19 market.

Key Debate: will the protein vaccine ever catch up?

In our view, the broader EUA language removes commercial overhang; The authorization for Novavax is in individuals 12 years or older who have either never been vaccinated or, importantly, been previously vaccinated with any original monovalent or bivalent COVID-19 vaccine. This represents a broader authorization versus the original monovalent vaccine, use of which was previously limited to individuals for whom an mRNA vaccine was not accessible/clinically appropriate or would have otherwise not elected to receive a COVID-19 booster. We therefore see a prior commercial overhang as removed, with the ball now in Novavax's court to execute on the guided ~$0.96-1.14B product sales in 2023 (we should get an update on uptake on full-year earnings call 1Q24e). Furthermore, we see commercial uptake as further complicated by the multi-dose format of Novavax vaccine, with each carton containing 10 doses (2 vials total) totaling ~$1,300 WAC price, with unused doses discarded if not used within 12 hours after first puncture. Therefore in a scenario where demand is low, we could see pharmacies delaying or electing not to stock the vaccine in subsequent months. Alternatively, pharmacies may only offer the Novavax vaccine on certain days of the week/month to concentrate administrations. Either way, with mRNA-based vaccines already off to a shaky start, we expect an uptick in 4Q23 product sales could lead to sharp declines in 1Q/2Q24 if vaccine demand remains low.

Notable 2024 clinical catalysts

2024 will likely be a drought of clinical catalysts for the already commercial biotech with the only notable event we can foresee near-term being the anticipated commencement of phase 3 COVID-19-Influenza Combination vaccine trial in 2024, which, although having the potential for accelerated approval, will not launch until 2026e at the earliest. Company goals for 2024 will remain on restructuring and further launch of its protein-based Covid vaccine and most near-term needle-driving catalyst will most likely be 2023 full-year earnings (1Q24e) which should provide further outlook into the future of Novavax.

Valuation / P&L thoughts heading into 2024

Things we will be focusing on for 1Q24 will be whether the company will be able to deliver on its promises including **1)** company guided 30-50 million dose market in US for 2023-2024 season, with potential for significant November and December vaccinations given fall/winter trends and later start as compared to 2022, **2)** reduced rate of spend/structural changes (important for potentially rebounding from "going concern"): with company guiding to reduced current liabilities by $128 million during 3Q23 and by approximately $1 billion as of 2023YE, and reduced year-to-date operating expenses through 3Q23e by $950 million, management says that the company is on track to exceed the previously announced global restructuring and cost reduction plan for 2023 by over $100M OpEx and prepared to initiate additional cost reductions of $300M, we will adjudicate whether the promises hold true come 1Q24e on the company's 2023 full-year earnings.

FDA: Food and drug administration

CDC: Center of disease control

C-19: Covid 19

EUA: Emergency use approval

Recursion

RXRX US – Rating: NEUTRAL (C-2-9) | PO: 14.00 USD | Price: 11.11 USD

What we expect for 2024: how much is enough to validate

Like other companies within the AI space, Recursion struggles with the same conundrum which is how to validate their platform. In our view, REC-3964 phase 1 topline appeared mostly positive with **1)** favorable safety profile (no SAEs/discontinuations), and **2)** favorable PK (7-10 hours half-life). That said, while we see the data as a preliminary signal of the platform heading in the right direction, more is likely needed to drive specialist investor attention with most likely focusing efficacy data expected in the phase 2 proof-of-concept study. Nevertheless, we see the initial safety/PK profile as promising and justifies the progression into further studies. Maintain Neutral and $14 PO.

Key debate: REC-3964 phase 2 important for validation

We note that nephrotoxicity, an AE prominent in vancomycin (drug used to treat C. diff.), was not present in the safety report of REC-3964, which we see as an additional stroke of confidence for the asset. With most prominent treatment-related AEs for '3964 being abdominal distension as well as flatulence, and no >Grade 1 AEs reported, we see the drug as so far being superior in safety as compared to vancomycin. That said, we caution that the sample size so far is still small (n=8 for each dose level) and note that a clear-cut conclusion on safety is still yet to be determined. We see the planned phase 2 proof-of-concept trial as making sense with a double-arm design (vancomycin vs. vancomycin + REC-3964) with the focus on subjects at risk for CDI with moderate to severe disease planning to receive SOC therapy. We expect efficacy and assessment of REC-3964's efficacy to be a primary focus in the phase 2 for investors. That said, we note key risk going forward being the difficulty with separating drug safety/efficacy effects when dealing with a combo treatment arm, which in this case includes vancomycin and REC-3964 (i.e. nephrotoxicity occurrence, an AE known for vancomycin, if discovered in the combo arm, cannot be attributed to either drug with certainty). While the design in our view is standard practice, we see more wood to chop to present data convincing enough to validate its AI platform.

Notable 2024 clinical catalysts

Upcoming catalysts include **1)** REC-3964 (phase 2 initiation 2024e **2)** REC-2282 (NF2): phase 2 safety/PK and preliminary efficacy in 2H24e **3)** REC-994 (CCM): phase 2 data in 2H24e. That said, we see the stock, over the course of 2023, trading very much more on partnerships and broad industry confidence other than clinical data. REC-3964 2023 readout was simply too little to be actionable and we expect 2024 to have a similar theme with true clinical derisking still 1-2 years away.

Valuation / P&L thoughts heading into 2024

Our $14 PO is based on a probability-adjusted NPV of Recursion's lead pipeline assets, including REC-4881 ($5/sh), REC-2282 ($3/sh), REC-994 ($2/sh), REC-3964 ($3/sh), and REC-3599 ($0/sh). We also assign value to platform and collaborations ($10/sh), as well as expenses for platform buildout (-$11/sh). We apply a 14% WACC (we project revenues out through 2038), in-line with other biotech companies of similar size and stage of clinical development. Current cash and equivalents contributes $2/share to our valuation. While we do acknowledge that valuing the AI-driven platform is difficult, we currently assess value for RXRX's platform/collaborations by triangulating opportunity cost, data storage cost as well as valuation based on deal premiums. Robust clinical data in our view could add a fourth pillar to add to the valuation of the platform, however, we do not see data near-term to be meaningful enough to drive shares.

AE: Adverse effects

RP2D: recommended phase 2 dose

SOC: Standard of care

CDI: C diff infections

BID: twice a day

PK: Pharmacokinetics

RegenxBio

RGNX US – Rating: BUY (C-1-9) | PO: 35.00 USD | Price: 17.40 USD

What we expect in 2024: '202 to highlight in DMD

We revisit 2023's key data points for '202 including **1)** patient aged 4.4 years old had expression level at 38.8%, **2)** patient aged 10.6 years old had expression level at 11.1%, **3)** tolerable safety profile with no SAE reported so far. In our view, the data shown is promising especially in the 4.4 yr old patient; while we see a notable reduction in the older children, our KOL checks say that children older than 7 are generally harder to treat with options limited, and given the progressive nature of DMD, muscle is harder to show functional improvement as the child ages. Furthermore, the fact that data presented were from dose level 1 (1x10^4 GC/kg) adds confidence in potential for expression levels to reach a clinically significant level as dose levels increase especially in older cohorts. In our view, non-inferiority is likely not needed, functional data will be able sufficient to approach FDA for approval. Our conversation with management also alluded to a plethora of data which can be expected in 2024e, including **1)** longer follow-ups on expression (6-mo, 12-mo etc.), **2)** NSAA functional data, **3)** time function test, **4)** care giver feedback, **5)** test of muscle strength, which we see as outcome measures that will take on more weight. With proof of non-inferiority likely not needed for the regulatory pathway, we see less pressure for '202 to "prove to be better" than comp, but rather focus on bettering itself. We reiterate Buy but lower our PO to $35 ($45 prior) to reflect lower-than-previously-projected platform royalties and increasing competitive scrutiny.

'314 Pivotal readout 2025e, becoming core investor focus

Expanded global enrollment in the phase 3 studies for RGX-314 delays anticipated regulatory filings to late-2025/1H26e (see our 1Q earnings takeaways); we see the additional sites in Europe, Japan, and Israel, as well as increased powering of the study, as ultimately strengthening the data package for RGX-314 (see our post-Angio thoughts here). We expect most investors focus now shifts to additional interm data and pivotal study start expected 2024e, which in our view is key to unlocking upside for shares.

Notable 2024 clinical catalysts

If looking at 2024 alone, DMD is the word. The '202 program is certainly receiving a lot of interest from investors especially given positive interim update (see our thoughts on the update here) and Elevydis recent approval from Sarepta (covered by Tazeen Ahmed). 202 vs Elevydis: expression similar, CT the differentiator. As a reminder, Elevydis from their topline results of Study 102 (part 1) demonstrated 12-week expression compared to baseline of 28.1%, as measured by western blot (n=20). In comparison, RGX-202 showed 38.8% expression from its 3-mo update (n=1, 4.4 yr old), which we consider to be at least in-line with Elevydis (although we do note n is small). Molecularly, we see both longer c-terminal domain and exon-skipping approaches as offering meaningful differentiation in terms of drug design (resembles closer to the actual micro-dystrophin gene) but expect the company will need to prove more in the clinic (including NSAA functional data, further expression data with longer follow-up, larger n) before investors give credit.

Valuation / P&L thoughts heading into 2024

Our $35/sh price objective is based on a probability-adjusted net present value (NPV) analysis of its four internal clinical programs, as well as royalties from partnered programs. Company sits on a comfortable cash position of ~$365M which should carry the company through upcoming value inflection points. We use a weighted-average cost of capital (WACC) of 10-12% and no terminal value (we project revenues through 2038), similar to other early-stage companies in our coverage universe. We ascribe $7 for RGX-314 in wAMD, $6 for RGX-202 in DMD, $0/$0 for MPS I/II, $13 for partnered programs, and approximately $9 for cash.

DMD: Duchene muscular dystrophy

CMO: Contract manufacturing organization

DR: Diabetic retinopathy

BLA: Biologic license agreement

nAb: neutralizing antibody

DRSS: Diabetic retinopathy severity scale

VEGF: vascular endothelial growth factor

wAMD: wet age-related macular degeneration

BCVA: best corrected visual acuity

QoL: Quality of life

H2H: Head-to-head

PoS: likelihood of success

Revolution Medicine

RVMD US – Rating: BUY (C-1-9) | PO: 34.00 USD | Price: 28.03 USD

What we expect in 2024: was the RAS data good or not?

ESMO readout NSCLC responses exceed our expectations at 38% in 2L+. Based on our previous analysis of SOC in 2L+ NSCLC, we have deemed 20-30% as the bar to beat for RMC-6236. With RMC-6236 yielding an ORR of 38% (1 CR, 14 PR, including three unconfirmed PRs), this is a strong case for '6236 efficacy in this patient population and line of therapy, in our view. Although KRAS G12C patients were excluded from the study, we also expect '6236 could have activity in KRASi-refractory patients given responses seen for RMC-6291 (RevMed's KRAS G12C asset) at the Triple meeting late last year (see our thoughts on the data). Overall, we see '6236's clinical profile as competitive versus chemotherapy in 2L+ NSCLC setting including docetaxel/ ninetadanib (4.7% ORR LUME-lung1, 50% VARGADO trial), which we see as potentially the ORR bar to beat versus placebo in the planned 2L+ phase 3 study, although note patient demographics could differ across studies. We upgrade our rating to Buy (from Neutral) and increase our PO to $34 ($31 prior) on growing confidence in the company's RAS(ON) platform heading into additional data updates in 2024 and recent positive data in our view helping to increase likelihood of success of key pipeline assets.

Key Debate: PDAC 20% ORR solid, but must be maintained

Our analysis of past efficacy data for SOC in 2L+ PDAC suggested 10-20% as the bogey for RMC-6236 in this particular indication. From the ESMO presentation, RMC-6236 was able to show for the first-time efficacy data for KRAS G12Dm 2L+ PDAC, a target previously considered "undruggable". In our view, considering that RMC-6236, being the first ever targeted therapy to show efficacy readout (excluding subgroup readouts), we see the data as matching our expectations. That said, we do note that the 20% ORR could go both ways from an investor's perspective, especially considering unconfirmed responders and data in comparison to reported chemo/targeted therapies ORR, including Gemicitabine/Capecitabine (19.4% vs 12.4% control), Keytruda (KEYNOTE-158 PDAC subgroup: 18.2% ORR). While we still see RMC-6236 phase 1/1b trial as the most convincing evidence of clinical activity to date in this specific, difficult-to-treat patient population, we note that a placebo-controlled trial comparing to SOC as likely needed to fully derisk the asset.

Notable 2024 clinical catalysts

While company has not guided to specific clinical catalysts in 2024, we expect interim readouts in 2024 for both RMC-6236 and RMC-6291, consisting of later cutoff date with hopefully longer duration of therapy. We note that '6291 would be an asset to watch in 2024 especially given preliminary potential shown at the Triple meeting for the asset, with future combo with cetuximab/SHP2 still on the table. Activity in G12C experienced patients is particularly impressive and, in our view, validating for the differentiated MOA. Expert checks say that future competitors in the G12C field will not necessarily need H2H trials to convince FDA but is certainly subject to comparisons with other G12C players which we expect to hold true heading into 2024.

Valuation / P&L thoughts heading into 2024

Our $34/share price objective is based on a probability adjusted sum of the parts (SOTP) net present value (NPV) of RevMed's pipeline therapies targeting RAS ($24/share, 70% of our valuation), SHP2/ SOS1 ($0/share). mTORC1/4EBP1 ($3/share), the early pipeline, which includes other KRAS targets (i.e., G12R, G12V, G13D, Q61X, etc.) ($0/share), and cash ($7/share). We currently assess a conservative PoS for both RMC-6236 an RMC-6291 (11-16% US) which we think could be conservative given strength of the data presented in 2023 at ESMO and the Triple meeting (see our thoughts on the data from ESMO, Triple meeting).

ORR: overall response rate

CR: complete response

PDAC: pancreatic adenocarcinoma

NSCLC: non-small cell lung cancer

2L: second line

KRAS G12X: kirsten rat sarcoma viral factor

SOC: standard of care

ESMO: European society of molecular oncology

DCR: disease control rate

PR: Partial response

KRAS G12D: Kirsten rat sarcoma viral oncogene G12D mutation

CRC: colorectal cancer

SD: Stable disease

PoS: Probability of success

SHP2: Src homology region 2 (SH2)-containing protein tyrosine phosphatase 2

AE: Adverse events

MOA: mechanism of action

FDA: Food and drugs administration

KOL: key opinion leader

RAS: Rat sarcoma viral factor

SpringWorks Therapeutics

SWTX US – Rating: BUY (C-1-9) | PO: 50.00 USD | Price: 38.4 USD

What we expect in 2024: two-drug company by end of '24

While focus remains on recent FDA approval of Ogsiveo, we see the company as much more than a one-trick-pony with the potential to introduce another approved drug, mirdametinib, to the market by early 2025 (especially given strong phase 2b data, see our thoughts on the data here). We see the positive on ReNue topline as effectively diversifying the narrative, and if in the worst case that Ogsiveo is unable to meet the bar set by investors in its commercialization, we see mirdametinib and the growing earlier pipeline as helping support shares over the next 12 months. In our view, with launch process of Ogsiveo fairly straight-forward (rare disease with clear unmet need should justify payor access and uptake), and mirdametinib as the encore, we think it is difficult to "short the launch" at least until a commercial trajectory becomes clearer. Maintain Buy and $45 PO.

Key Debate: Mirdametinib approval diversifies narrative

Phase 2b ReNeu data gave us a topline look at mirdametinib ahead of NDA filing expected to commence in 1H24e. Overall, we see the topline update as promising given **1)** encouraging efficacy profile (52% ORR in pediatric, 41% ORR in adult) clearly better than the single other competitor (Koselugo ORR: 44% in pediatric). **2)** Safety profile for mirdametinib demonstrated fewer TEAEs including Gr3+ rash (4%) diarrhea (2%) as well as less dose interruptions/reductions/discontinuations in comparison to AstraZeneca's Koselugo (Exhibit 1). **3)** mirdametinib being first treatment for NF1-PN adult patients in our view raises the ceiling on the market opportunity if approved (Koselugo 3Q23 global sales were $87M, our model projects ~$1.5B peak sales for mirda assuming approval in both pediatric and adult markets and a modest 8% peak share in NF1). We therefore see multiple boxes being checked from ReNue. Together, SpringWorks' goal of introducing two approved assets onto the market in the next 18 months is becoming more tangible.

Notable 2024 clinical catalysts

Ogsiveo launch and mirdametinib submission are in focus. And while we expect the conversation will revolve around Ogsivio sales in 2024, we see growing attention to mirdametinib as well. Depth of response from ReNue is a parameter which we consider to be an important differentiating factor when mirda is compared with Koselugo heading into 2024 (we think, similar to what the company did for Ogsiveo, SWTX will provide QoL data in support of filing). Median depth of volumetric response for mirda was over 40% in both cohorts (significant number of responses also seen deeper than 80%), which in our view compares favorably with Koselugo where median depth of response has been under the 30% mark (not to mention the usage of local review, which is less stringent than BICR used in ReNeu). Positive PRO in our view (see our last conversation with management) also ultimately contributes to patient stickiness and compliance. While management has stated that analysis has not yet been carried out on PRO data, QoL improvements, pain management and other sorts of symptoms management, these are key points for ultimate commercial uptake in our view (details expected at an upcoming medical meeting 1H24e).

Valuation / P&L thoughts heading into 2024

Our $50/share price objective is based on a probability-adjusted net present value (NPV) for nirogacestat mono ($23/share), nirogacestat combo ($2/share), mirdametinib ($12/share), BGB-3245 ($1/share), TEAD inhibitor program ($1/share), EGFR inhibitor program ($1/share), and cash ($8/share). We apply probabilities of success from 3% (EGFR, TEAD) to 76% (nirogacestat EU), a weighted-average cost of capital (WACC) of 10-13%, and -4% (nirogacestat) to -1% (early pipeline) terminal growth rate.

PDUFA: Prescription drug user free act

ORR: Overall response rate

FDA: Food and drugs administration

NF1-PN: neurofibromatosis type 1

ORR: Overall response rate

PRO: patient-reported outcomes

BICR: blinded-independent central review

NDA: new drug application

Gr3: Grade 3

QoL: quality of life

TG Therapeutics

TGTX US – Rating: UNDERPERFORM (C-3-9) | PO: 7.00 USD | Price: 18.02 USD

What we expect in 2024: Briumvi launch curve takes shape

TGTX shares made a resurgence in December (+21.2%; NBI: +15.7%), which we see as likely driven more by negative lateral news from BTK developers (a fringe overhang from our KOL discussions), short covering dynamics, and broader sector strength than a change in the company's core fundamentals (see our latest sensitivity analysis). With more than a year of sales under its belt and new launch volatility (J code, payor on-boarding, free drug) becoming less of a factor, we anticipate the true demand curve for Briumvi will likely begin to emerge over the next 12 months. Looking to 2024, we expect the debate around RMS market opportunity for Briumvi will continue, with a keen investor focus on quarterly sales and company commentary around alternative launch metrics (scripts filled, % new centers/prescribers, demographic of patients going on therapy, etc.). But until we see additional evidence of Briumvi's competitive differentiation (esp. with a subq Ocrevus launch expected late-2024/early-2025), we remain reserved on the market setup for Briumvi. Reiterate Underperform and raise PO to $7 (from $6 prior) on slower ramp-down in outer years after patent runs out.

Key debates: what is the true market oppty for Briumvi?

We see 4Q/FY23 earnings and, more importantly, 2024 guidance and 1H24 sales as key pivot points for TGTX shares in the near-term. With 4Q assuming a roughly linear step up from 3Q ($36M BofAe, +44% q/q; -$0.4M cons) and recently provided 2023 guidance, we expect TG will at least meet the company's 2023 sales range of $82-86M ($84.7M BofAe; -$0.4M cons). Consensus for 1Q24 ($as43M, +18% q/q) also looks achievable if 2023 guidance is met, although we are below street for full-year 2024 ($174M; -$39.3M cons) given our view on a modest slow-down in growth over the course of the year, in-line with current trends on slowing scripts per physician (see our 3Q earnings thoughts). Looking to the mid- to long-term, we see current consensus as underselling the potential impact of an Ocrevus subq, with a 34% 5-year forward sales CAGR for Briumvi appearing high in our view, with our modeled 25% CAGR already accounting for cumulative economics (assuming long duration on therapy) and growing CD20 class.

Notable 2024 clinical catalysts

With TG no longer sharing distributor-level data with third-party companies, we expect an increased emphasis will be placed on prescriber feedback, company commentary, and quarterly sales numbers in 2024. Key metrics we'll be watching include: **1)** sales growth, **2)** repeat use at the prescriber level, and **3)** new patient demographics. We see potential approval of Ocrevus subq (Roche, covered by Sachin Jain) in late-2024e/early-2025e as a negative catalyst for TG (see our phase 3 Ocrevus subq data read-through). While we agree that the CD20 subq market is likely separate from IV at an individual prescriber level, we expect subq to have an outsized share of the CD20 class growth. It can offer more covenience (with maintained efficacy vs IV) for prescribers/patients. Beyond RMS, TG also lists 1801 (anti-CD47/19 bispecific) and 1701 (BTK inhibitor) in their pipeline, although given recent guidance to cashflow breakeven we expect limited additional investments into these programs in the near-term.

Valuation / P&L thoughts heading into 2024

Majority of our $7 PO comes from ublituximab, which we value at $6/sh, reaching peak sales of ~$791M in 2031. Given our conservative view on prescriber uptake as well as stickiness of patients, we see the drug achieving a slower-than-expected ramp to peak. Ex-US commercialization agreement with Neuraxpharm (total deal size: $645M; $150M in upfront and near-term milestones; projected up to 30% in tiered royalties), in our view, adds comfort to TG's cash position (pro-forma cash of approximately $285M). That said, we expect the deal lowered total valuation for Briumvi for many investors (although note that cost reductions/synergies could also be realized).

RMS: Relapsing multiple sclerosis

Subq: subcutaneous

IV: intravenous

BTK: Burton's Tyrosine Kinase

Xencor

XNCR US – Rating: BUY (C-1-9) | PO: 34.00 USD | Price: 22.11 USD

What we expect in 2024: vudalimab prostate data in focus

For most of 2023, XNCR shares (-18.4%; NBI: +4.7%) traded in-line with the broader biotech sector primarily, in our view, driven by a lack of actionable clinical data catalysts. And while we expect many continue to wait for meaningful derisking from the XmAb platform before assigning higher valuation, we see Xencor's recent BD activities (Ultomiris deal) paired with pipeline reprioritizations as shoring up cash position (~$650M pro forma cash and equivalents) ahead of what's shaping up to be a productive 2024. We see a positive setup ahead of key data updates including vudalimab phase 2 prostate data (early-2024e), XmAb819 (ENPP3xCD3 for kidney cancer), and xaluritamig (AMG 509, STEAP1xCD3 for prostate). Reiterate Buy and lower PO to $34 (from $37 prior) on updated year-end 2023 cash offset by adjusted expected partnership revenues.

Key debates: where/when does the XmAb platform inflect?

While we are of the view that Xencor's platform (internal pipeline, current/future partnerships) is currently undervalued, we expect prior competition issues in developing drugs against Xencor's targets (ICOS, ENPP3, IL2, CD20) remains an overhang for the company's programs heading into 2024. Therefore, the next leg up for XNCR shares are likely to come from either concretely-positive phase 2 prostate data from vudalimab and/or cumulative platform derisking from earlier clinical assets (xaluritamig, XmAb819, XmAb541). That said, we see Xencor as continuing to be strategic around allocation of capital to areas with highest ROI (vudalimab 1L NSCLC study start, XmAb104 study stop, XmAb306 agreement update with Roche/Genentech, etc.). Xencor's strengths, including high quality assets with long IP runways and the proprietary XmAb platform which underpins its validating external partnerships, should unlock additional value for shares as the company steps through data catalysts over the next 12-18 months

Notable 2024 clinical catalysts

We see the key near-term data catalyst for Xencor as being clinical data for vudalimab from the company's phase 2 prostate cancer study (monotherapy and in combination with chemo or PARP inhibition) at a medical conference in early 2024. And while the company doesn't typically guide to data catalysts, we see below as our areas of near-term focus: Vudalimab phase 1b/2 1L NSCLC chemo combo study start (imminent), vudalimab monotherapy phase 2 prostate cancer data (early-24e), XmAb819 (ENPP3) for kidney cancer phase 1 dose escalation and RP2D selection (2024e), XmAb541 (CLDN6xCD3) phase 1 study start (1H24e), additional phase 1 xaluritamig (AMG 509, STEAP1xCD3) data/follow-up (2024e).

Valuation / P&L thoughts heading into 2024

While vudalimab remains Xencor's lead asset and is likely to continue to be the biggest near-term focus for investors ($7/sh in our model), the company currently has 10 additional assets in the clinic ($10/sh cumulatively) with two more (XmAb662, XmAb541) starting phase 1 studies near-term. Xencor's partnerships ($9/sh) provide royalty revenue/milestone streams at very little cost to Xencor and further validates the company's technology, in our view. Current valuation in our view underappreciates the market opportunity for vudalimab in prostate/ovarian cancers (20% of our valuation) and out-licensed royalty streams (28% of our valuation). Indeed, we see success of only 1-2 pipeline therapies (Xencor has 10+ clinical assets) and/or new partnerships as not fully reflected in shares currently. Furthermore, we assign relatively high peak penetration rates (15-20%) across the in-house pipeline given what we see as first-in-class or best-in-class potential for many of Xencor's assets. We therefore see a relatively low bar for Xencor to raise the ceiling on valuation near-term, however this will likely be dependent on concretely-positive clinical data from the pipeline.

BD: business development

ROI: return on investment

1L: front-line

NSCLC: non-small cell lung cancer

IP: intellectual property

PARP: poly (ADP-ribose) polymerase

RP2D: recommended phase 2 dose

Y-mAbs Therapeutics

YMAB US – Rating: NEUTRAL (C-2-9) | PO: 10.00 USD | Price: 6.85 USD

What we expect in 2024: Goals clear, now time to execute

Y-mAbs enters 2024 with a relatively clear set of objectives: **1)** continue to push Danyelza market uptake and growth, **2)** unlock value from SADA through a combination of clinical data updates and potential partnerships (see our 2H23 outlook report). And while we see opportunity for the company to execute on both fronts (our thoughts following 3Q23 earnings), recent sales/scripts for Danyelza appear to be plateauing (stabilizing at ~$20M in quarterly sales) and SADA programs are still early (GD2-SADA phase 1 progressing, CD38-SADA IND cleared). That said, ex-US Danyelza expansion as well as label expansion into 1L pediatric neuroblastoma and 2L osteosarcoma could add to the market opportunity in the near- to mid-term. We therefore look for continued progress from the Danyelza launch and additional PK/response data for SADA programs before getting more positive on the Y-mAbs story. Maintain Neutral and $10 PO.

Key debates: Is the market for Danyelza saturated?

Danyelza sales remained roughly flat throughout 2023 ($20.3M 1Q23, $20.8M 2Q23, $19.9M 3Q23), which we see as driven by a combination of flat r/r NB incidence, slower rate of penetration outside of MSK, and balance of patients coming on/going off therapy across activated centers. Heading into 2024, we expect the key debate will still revolve around Danyelza topline contribution, which can see an uptick in numbers as label expansion happens with data readout supporting expansion into 1L neuroblastoma/2L osteosarcoma expected likely next year. And while the company's implied 10% y/y growth rate in new cash runway guidance could be conservative, we expect this is likely below what many investors were hoping for the launch. We look for a turnaround in growth from the new Danyelza marketing campaign set to begin in 2024.

Notable 2024 clinical catalysts

We expect a more fulsome data update from the phase 1 GD2-SADA study to come at a major medical meeting in 2024, which should include safety, PK data, biodistribution data, and initial tumor imaging data across at least 9 patients from the first 3 dose cohorts. The POC data presented during the company's 3Q earnings call, including tumor enrichment and PK exposure, were in our view promising, but very early. We expect the larger data update from the program in 2024 will be more actionable for investors. Additional updates from the pipeline we expect over the next 12-month include: **1)** updates on US and ex-US (China, EU, Mexico, Brazil, etc.) Danyelza launches, **2)** CD38-SADA study start in r/r NHL and enrollment, **3)** Danyelza relapsed osteosarcoma data and phase 2 Study 205 IND submission (3Q24e).

Valuation / P&L thoughts heading into 2024

Our $10/sh PO is broken down roughly into $7/sh for Danyelza, $0/sh for omburtamab (we adjusted PoS from 100% to 0% since FDA CRL), $1/sh for the earlier pipeline (SADA, GD2-GD3 vaccine, etc.), and $2/sh cash. The company has guided that cash runway from its ~$87M cash and equivalents (ended 3Q23) and $80-85M in 2023 Danyelza revenues should support operations into mid-2027. This cash burn guidance could, in our view, be conservative as it assumes a 10% y/y growth in Danyelza from 2024-2026 and no new partnerships or BD income. Based on our model estimates, we expect 2024 Danyelza sales to have YoY growth rate of 31% and reach ~$106M (+$5M cons) for the full year. That said, Danyelza must meaningfully outperform consensus to change the narrative for shares, in our view.

SADA: Self-assembling and de-assembling

1L: Front line

r/r: relapse/refractory

2L: Second line

GD2: disialoganglioside

NB: Neuroblastoma

PK: pharmacokinetics

FDA: Food and Drug Administration

CRL: complete response letter

BD: business development

Investment Rationale

Erasca
We rate Erasca Neutral. While Erasca provides a compelling approach to address KRAS-pathway-driven tumors with clear expertise in the management team, the data readout has been mostly sub-par in terms of efficacy shown by response rates. That said, we do see promise in the pipeline given the sheer depth it has, but value inflection has yet to happen in our view

Exscientia
We rate Exscientia Neutral. While we think its unique tech platform differentiates it from other biotechnology companies, AI-driven drug discovery platforms will likely not receive the validation many investors hope for in the near-term. We do note Exscientia has multiple assets in the pipeline and the potential to bring more forward at a lower cost and faster speed than most peers which in our view could be a differentiating factor. That said, value-add to stock is unlikely to happen near-term.

Revolution Medicines
We rate RVMD Buy, given a promising readout in our view recently at ESMO 2023 and Triple meeting 2023 on its two lead assets. That said, we see promise in the RAS(ON) platform as the new spearhead for the pipeline, with broad potential for the company's assets (peak sales >$5B) driving upside to our valuation if additional monotherapy or combination activity is shown in the clinic.

Price objective basis & risk

Day One Biopharmaceuticals (DAWN)
Our $10/share price objective is based on a probability adjusted NPV for tovorafenib in r/r pLGG ($2/sh), tovorafenib for 1L pLGG ($1/sh), tovorafenib for RAF-driven solid tumors ($1/sh), pimasertib/tovorafenib combo for RAF-driven solid tumors ($1/sh), and cash ($5/sh). We apply a WACC of 10-12% and 1% (tovorafenib) to 3% (pima/tovo combo) terminal growth rate.

Downside risks to our PO are: 1) FDA red flags FIREFLY-1 trial design and delays tovorafenib approval, 2) lack or urgency for FDA to approve tovorafenib given high survival rate for current pLGG patients, 3) new RANO-LGG endpoint can result in lower ORR than previously reported, 4) D+T combo presents as further competition with randomized trial design setting a bar hard for tovorafenib to reach, 5) lack of platform innovation with all assets acquired could mean potential for future lacking, 6) small end market size can affect topline contribution even with approval, 7) rapidly expiring patents for pimasertib can give room for biosimilars to erode market share

Upside risks to our PO are: 1) FDA approves tovorafenib with no delays given unmet need and compelling data package, 2) BRAF-driven solid tumors substudy trial continues to readout positively, 3) FIREFLY-2 phase 3 pivotal for 1L pLGG reads out positively and earlier than expected, 4) clear pipeline strategy and potential for future synergy in combos starting with pimasertib/tovorafenib, which opens up larger market in solid tumors.

Erasca (ERAS)
Our $6/share price objective is based on a probability adjusted NPV of naporafenib ($2/sh), ERAS-007 ($1/sh), ERAS-601 ($0/sh), ERAS-1/4 ($0/sh), ERAS-801/12 ($0/sh), the discovery pipeline ($1/sh), and cash ($2/sh). We apply a WACC of 11-16% and -5% to 3% terminal growth rate.

Downside risks: 1) expanded clinical studies for ERAS-007 fail to replicate prior safety and efficacy data, 2) pipeline therapies fail to demonstrate activity as monotherapy, 3)

competitors produce more convincing data for competing therapies, 4) funding is insufficient to move forward pipeline aspirations or manufacturing buildout, 5) MAPKlamp strategy still fails to address majority of cancer patients.

Exscientia (EXAI)
Our $9 PO is based on a probability-adjusted net present value (NPV) of Exscientia's lead pipeline assets, as well as value assigned to the early-stage assets, the Bristol Myers Squibb collaboration, and the underlying technology platform itself. We apply a 15% weighted-average cost of capital (WACC, we project revenues out through 2040), in line with other biotech companies of similar size and stage of clinical development.

Upside risks would come from pipeline updates or further external validation of the platform.

Downside risks are competition, drug development uncertainty, revenue volatility, and lack of profitability/potential need for further capital.

HUTCHMED (HCM)
Our PO of $29 is derived from a probability-adjusted net present value (NPV) analysis, including $7/share for savolitinib, $10/share for fruquintinib, $4/share for surufatinib, $1/share for amdizalisib, $1/share for sovleplenib, -$2/share for other pipeline assets, $3/share for the commercial platform and $5/share for net cash. We use a weighted-average cost of capital (WACC) value ranging from 7% (commercial platform) to 11% (future pipeline) and terminal value ranging from -5% (legacy business) to 2% (future pipeline).

Downside risks to our price objective are 1) unfavorable efficacy and/or safety data for savolitinib, fruquintinib and surufatinib in clinical trials, 2) weaker-than-expected revenue for commercial platform, and 3) earlier-than-expected or more-than-expected competition for the above-mentioned three leading clinical assets.

Immatics (IMTX)
Our $16/share price objective is based on a probability adjusted NPV of lead TCR-T ACTengine programs including IMA201 ($0/share), IMA402/401Bispecifics ($4/share), IMA203 ($7/share) and cash and equivalents which contributes $5/share. We apply a WACC of 12% given novel nature of Immatics' platform and no terminal value (we project out revenues through 2035).

Downside risks: 1) lead assets IMA203 do not show an effect in early stage clinical studies or fail to reproduce findings in large pivotal trials, 2) Immatics' programs fail to exhibit differentiation versus competitors (cell therapies, approved cancer drugs), 3) challenges in manufacturing and commercial scalability limit clinical adoption, 4) reimbursement/pricing headwinds shrink margins on approved therapies, 5) funding is insufficient to move pipeline aspirations forward, 6) termination of collaboration agreements by partners due to shifting priorities, 7) dilution risk from additional equity financing expected to be required to advance clinical programs.

Krystal Biotech (KRYS)
Our $140/share price objective is based on a probability-adjusted net present value (NPV) for rare dermatology ($107/share), respiratory, including cystic fibrosis (CF) and AATD ($9/share), aesthetics through the Jeune subsidiary ($6/share), the discovery pipeline ($4/share), and cash ($14/share). We apply probabilities of success from 9% (aesthetics) to 100% (Vyjuvek), a weighted-average cost of capital (WACC) of 10-13%, and -3% (rare derm) to 2% (early pipeline) terminal growth rate.

Downside risks: 1) Vyjuvek launch uptake slower than anticipated, 2) HSV-1 technology fails to yield compelling data in expanded chronic indications, 3) competitors produce

more convincing data for competing therapies, 4) regulatory and/or reimbursement landscape changes unfavorably for gene therapies, and 5) funding is insufficient to move forward pipeline aspirations or further commercial/manufacturing build out.

MeiraGTx (MGTX)
Our $15/share price objective (PO) is based on a probability-adjusted NPV of multiple assets including AAV-RPE65 in RPE65 retinal dystrophy ($2/share), AAV-CNGB3 ($1/share), AAV-CNGA3 ($1/share) in achromatopsia, AAV-RPGR in X-linked retinitis pigmentosa ($0/share) and AAV-hAQP1 in xerostomia ($5/share), AAV-GAD in Parkinson's ($1/share), gene regulation platform ($4/share) and $1/share in cash. We apply probabilities of success ranging from 5% (riboswitch) to 30% (AAV-RPGR for XLRP), use a WACC of 10%-12%, and terminal values ranging from -5% (RPE65) to -1% (gene regulation platform) with revenues projected through 2038.

Downside risks: 1) failure of early clinical trials, 2) emergence of safety signals, 3) failure of partnered programs, and 4) commercialization failures.

Novavax (NVAX)
Our $4/sh price objective is based on probability-adjusted net present value (NPV) of lead assets Nuvaxovid ($-3/share), NanoFlu ($2/share), ResVax ($0/share), other pipeline (-$1/share), and cash ($6/share). We use a weighted-average cost of capital (WACC) of 10-13% and terminal values ranging from -12% (COVID-19) to 2% (other pipeline). We apply probabilities of success including 100% for Nuvaxovid in EU/ROW, 64% for NanoFlu, 7% for ResVax, and 4% for other pipeline.

Upside risks: 1) Nuvaxovid use could be stronger than expected, 2) assets in flu, RSV, and malaria may find a path to regulatory approval, 3) additional pipeline candidates may be nominated for novel disease areas, 4) competing therapies may show worse-than-expected efficacy/safety.

Downside risks: 1) omicron efficacy and heterologous boost benefit could wane, 2) Nuvaxovid revenue durability may miss consensus' high expectations, 3) sustained operating expense may erode profits, 4) regulatory path unclear for RSV/flu, 5) competition across pipeline disease areas could continue to intensify, 6) lack of early pipeline could leave a profitability gap 2023-2027.

Recursion Pharmaceuticals, Inc. (RXRX)
Our $14 PO is based on a probability-adjusted NPV of Recursion's lead pipeline assets, including REC-4881 ($5/sh), REC-2282 ($3/sh), REC-994 ($2/sh), REC-3964 ($3/sh), and REC-3599 ($0/sh). We also assign value to platform and collaborations ($10/sh), as well as expenses for platform buildout (-$11/sh). We apply a 14% WACC (we project revenues out through 2038), in-line with other biotech companies of similar size and stage of clinical development. Current cash and equivalents contributes $2/share to our valuation.

Upside risks would come from pipeline updates or further external validation of the platform.

Downside risks to our PO are: 1) clinical trial failures, 2) better than expected data from competitors, 3) dilution from cash raises.

Regenxbio, Inc. (RGNX)
Our $35/share price objective is based on a probability-adjusted net present value (NPV) analysis of its four internal clinical programs, as well as royalties from partnered programs. We use a weighted-average cost of capital (WACC) of 10-12% and no terminal value (we project revenues through 2038), similar to other early-stage companies in our coverage universe. We ascribe $7 for RGX-314 in wAMD, $6 for RGX-202 in DMD, $0/$0 for MPS I/II, $13 for partnered programs, and approximately $9 for

cash.

Downside risks: 1) failure of ongoing clinical trials, 2) emergence of untoward safety signals, 3) failure of partnered programs which reduces economics owed to Regenxbio, 4) difficulties in commercializing gene therapies, 5) manufacturing issues as capabilities are brought in house, 6) litigation risk that could jeopardize the NAV platform IP estate or cause undue legal/court fees.

Revolution Medicines (RVMD)
Our $34/share price objective is based on a probability adjusted sum of the parts (SOTP) net present value (NPV) of RevMed's pipeline therapies targeting RAS ($24/share), SHP2/ SOS1 ($0/share), mTORC1/4EBP1 ($3/share), the early pipeline, which includes other KRAS targets (i.e., G12R, G12V, G13D, Q61X, etc.) ($0/share), and cash ($7/share, 44%). We apply a weighted-average cost of capital (WACC) of 10-13%, -5% to 2% terminal growth rate, and probabilities of success ranging from 16% (RAS) to 6% (early pipeline).

Upside risks: 1) RMC-4630 (SHP2) shows meaningfully better activity in combination, 2) additional responses are demonstrated for RMC-5552 (mTORC1) in subsequent data updates, 3) RAS(ON) studies recruit faster than anticipated or find an accelerated path to market, 4) competing therapies show worse-than-expected efficacy/safety.

Downside risks: 1) lackluster SHP2 monotherapy data could expand to company's other pipeline assets, 2) RAS(ON) assets experience delays in clinical development slowing their path to market, 3) data from competing therapies is better than expected, 4) unexpected safety issues for mTORC1, SHP2, or RAS narrows the therapeutic window, 5) regulatory outlook worsens, slowing path to market (i.e. accelerated approval).

SpringWorks (SWTX)
Our $50/share price objective is based on a probability-adjusted net present value (NPV) for nirogacestat mono ($23/share), nirogacestat combo ($2/share), mirdametinib ($12/share), BGB-3245 ($1/share), TEAD inhibitor program ($1/share), EGFR inhibitor program ($1/share), and cash ($8/share). We apply probabilities of success from 3% (EGFR, TEAD) to 76% (nirogacestat), a weighted-average cost of capital (WACC) of 10-13%, and -4% (nirogacestat) to -1% (early pipeline) terminal growth rate.

Downside risks are: 1) nirogacestat regulatory review experiences setbacks or final label is more limited than expected, 2) nirogacestat launch delayed or uptake slower than anticipated, 3) nirogacestat fails to yield compelling data in combination with BCMA therapies, 4) competitors produce more convincing data for competing therapies, 5) regulatory and/or reimbursement landscape changes unfavorably, and 6) funding is insufficient to move forward pipeline aspirations or further commercial/manufacturing build out.

TG Therapeutics (TGTX)
Our $7/share price objective is based on a probability adjusted NPV for ublituximab ($6/sh), TG1801 ($0/sh), and cash ($1/sh). We apply a WACC of 10-13% and -3% (ublituximab) to -5% (TG1801) terminal growth rate.

Downside risks are: 1) ublituximab efficacy data not promising in comparison with control arm, 2) hour-long infusion time not a sufficient convenience differentiator, 3) vaccine tolerance and infection rate still a concern for anti-CD20s, 4) switch from current anti-CD20 unlikely, 5) discounted pricing feasibility diminishing, 6) lack of early pipeline value leaves uncertainty for 2023-2026 , 7) complete oncology pipeline disbandment may induce further concerns.

Upside risks are: 1) ublituximab launch could be stronger than expected, 2) ublituximab

approval could induce more-than-expected strength in shares, 3) pipeline synergy means possibility for combos, 4) cost reduction/synergies with deleted oncology pipeline might yield positives.

Xencor (XNCR)
Our $34/share price objective is based on a probability-adjusted net present value (NPV) for vudalimab ($7/sh), plamotamab royalties ($0/sh), XmAb306 ($2/sh), XmAB104 (-$1/sh), XmAb564 ($2/sh), XmAb819 ($2/sh), XmAb808 ($2/sh), XmAb968 ($1/sh), XmAb662 ($1/sh), XmAb541 ($1/sh), partnered programs ($9/sh), and cash and equivalents ($9/sh). We apply probabilities of success ranging from 6% (XmAb968) to 20% (vudalimab), a weighted-average cost of capital (WACC) of 11-14%, and -5% to 0% terminal growth rate.

Downside risks: 1) Clinical studies fail to yield viable drug profiles or validate preclinical observations, 2) a decline in partnership royalties creates a near-term revenue trough, 3) Xencor therapies against historically challenging targets fail to be competitive, 4) licensed assets miss endpoints in clinical studies or are deprioritized by partners, 5) Xencor fails to strike new partnership/licensing deals for XmAb platform, and 6) funding is insufficient to move forward pipeline aspirations or further commercial/manufacturing build out.

Y-mAbs Therapeutics, Inc (YMAB)
Our $10 price objective is based on a probability-adjusted net present value (NPV) of lead assets omburtamab ($0/share) and naxitamab ($7/share), early pipeline, including GD2xCD3 and SADA platform ($1/share), and cash approximately ($2/share). We apply probability of approvals from 6%-16% (early platform) to 55% (Danyelza in 1L Neuroblastoma), a weighted average cost of capital (WACC) of 10-13%, and terminal growth rate of -1% to -3%.

Upside risks: 1) Danyelza sales outperform projections, 2) Danyelza label expansion successful, 3) SADA platform encouraging clinical data

Downside risks: 1) failure of late-stage clinical trials, 2) emergence of safety signals, 3) slow clinical adoption, and 4) commercialization failures.

Analyst Certification

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

US - Biopharmaceuticals Coverage Cluster

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

US - Biopharmaceuticals Coverage Cluster

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

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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.

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

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

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