

## US Biopharmaceuticals

## AACR 2024 Preview: What to look for in our coverage (RVMD KRY5 HCM)

Price Objective Change

Companies across our coverage will be presenting at AACR 2023, we summarize interesting presentations to watch and our key observations >>>

**RVMD: deeper look into preclinical pipeline**

RVMD's robust preclinical pipeline will highlight presentations at AACR 2024. We focus on our top three most interesting presentations in our view from the weekend including **1)** RMC-4550 oral presentation on immune rejection of KRASG12C inhibitor-resistant subpopulations in lung cancer (**Abstract #1214**) **2)** RMC-7977 oral presentation on anti-tumor activity and immune effects of the RASMULTI(ON) inhibitor in preclinical models of NRAS-mutant melanoma (**Abstract #1217**) **3)** Presentation on RMC-5127, RASG12V(ON) inhibitor in preclinical model (**Abstract #3340/28**). While we see most investor attention remaining on clinical assets, preclinical pipeline, while unlikely to drive shares near-term, can add confidence to RVMD's core technological approach. Maintain Buy and \$34 PO.

**KRY5: KB707 expands the pipeline potential**

After KB707 IND was announced July 2023 ([see our thoughts on the announcement here](#)), the addition of KB707 (HSV-based vector delivery of IL-2 and IL-12) to the KRY5 story is in our view injecting further confidence in the future pipeline potential as the company ventures into the oncology field. The KB707 program will be 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. With the FDA accepting an IND to evaluate intra-tumoral KB707 in patients with solid tumors, key catalyst coming up is interim data which is expected in 2024e. Presentation at AACR in our view is unlikely to drive shares given its preclinical focus on mechanism of action of the drug class hence we expect investor focus to remain on the upcoming clinical data (Aesthetics: KB301 1H24e). Reiterate Buy and raise PO to \$200 (\$168 prior) given advancing progress for the KB707 asset.

**HCM: deeper look at syk, preclinical pipeline bolstered**

Three presentations for HUTCHMED to highlight at AACR 2024: **1)** Presentation on HMPL-523 (syk inhibitor) in patients with r/r lymphoma (**Abstract #CT114/23**) which in our view could be interesting as the company continues to bolster its future pipeline, **2)** Presentation on savo/osi in patients with EGFRm/METamp NSCLC (**Abstract #CT251**) which should provide further evidence on savolitinib's potential as a combo partner, **3)** efficacy of suru/sintilimab in phase 2 study (**Abstract #CT266**). While we do not expect the stock to move from these presentation, we continue to like the HUTCHMED story. Maintain Buy and \$29 PO.

See our AACR 2024 Planner on Page 2 >>>

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Equity  
United States  
Biopharmaceuticals

**Alec W. Stranahan**  
Research Analyst  
BofAS  
+1 646 743 2109  
[alec.stranahan@bofa.com](mailto:alec.stranahan@bofa.com)

**John Fan** >>  
Research Analyst  
Merrill Lynch (Canada)  
+1 917 634 7972  
[john.fan@bofa.com](mailto:john.fan@bofa.com)

**Abbreviations:**

**KOL:** Key opinion leader

**HSV:** Herpes virus

**IL-2/IL-12:** Interleukin-2/12

**IND:** Investigational new drug

**AE:** Adverse effects

**KRAS G12D:** Kirsten rat sarcoma viral factor glycine to aspartic acid codon 12

**NRAS:** neuroblastoma RAS viral (v-ras) oncogene homolog

**r/r:** relapsing

**NSCLC:** non-small cell lung cancer

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**Exhibit 1: AACR 2024 Planner**

We summarize key presentations to watch for at AACR 2024

Company	Program	Stage	Day	Time (PST)	Type	Abstract No.	Titles	Importance
<b>April 7th (Sunday)</b>								
Revolution Medicine	RMC-6236	Preclinical	April 7th	1:30pm	Poster	<u>581 / 4</u>	Identification of potential biomarkers of response to RASMULTI(ON) plus anti-PD-1 combination in preclinical PDAC models	Low
Revolution Medicine	RMC-4550	Preclinical	April 7th	3:05pm	Oral	<u>1214</u>	Investigating therapeutic strategies to promote immune rejection of KRASG12C inhibitor-resistant subpopulations in lung cancer	Low
Revolution Medicine	RMC-7977	Preclinical	April 7th	3:50pm	Oral	<u>1217</u>	Defining the anti-tumor activity and immune effects of the RASMULTI(ON) inhibitor RMC-7977 in preclinical models of NRAS-mutant melanoma	Low
<b>April 8th (Monday)</b>								
Day One Biopharmaceuticals	Tovorafenib	Preclinical	April 8th	9am	Poster	<u>1972 / 21</u>	Preclinical activity of the type II RAF inhibitor tovorafenib in tumor models harboring either a BRAF fusion or a NF1-LOF mutation	Low
Revolution Medicine	RMC-6272	Preclinical	April 8th	9am	Poster	<u>1443 / 14</u>	The PI3K-AKT-mTOR axis persists as a therapeutic dependency in KRASG12D-driven non-small cell lung cancer	Low
Revolution Medicine	RMC-5127	Preclinical	April 8th	1:30pm	Poster	<u>3340 / 28</u>	RMC-5127, a first-in-class, orally bioavailable mutant-selective RASG12V(ON) inhibitor is central nervous system (CNS)-penetrant and demonstrates anti-tumor activity in a preclinical intracranial xenograft model	Low
HUTCHMED	HMPL-523	Phase 1	April 8th	1:30pm	Poster	<u>CT144 / 23</u>	Safety and efficacy of HMPL-523 (Syk inhibitor) in patients with relapsed or refractory lymphoma	Medium
HUTCHMED	HMPL-295	Preclinical	April 8th	9am	Poster	<u>1661 / 8</u>	1661 / 8 - Preclinical characterization of HMPL-295, a potent and selective ERK 1/2 inhibitor	Low
HUTCHMED	HMPL-506	Preclinical	April 8th	9am	Poster	<u>2113</u>	2113. HMPL-506, a novel, highly potent and differentiated menin-MLL inhibitor for the treatment of MLL-rearranged and NPM1 mutant acute leukemia in preclinical models	Low
HUTCHMED	Surufatinib	Preclinical	April 8th	9am	Poster	<u>2126</u>	2126. Efficacy and underlying mechanisms of surufatinib in non-small cell lung cancer treatment	Low
HUTCHMED	Surufatinib	Preclinical	April 8th	9am	Poster	<u>2127</u>	2127. Enhancing radiosensitivity in biliary tract cancer: The dual role of surufatinib in tumor suppression and macrophage reprogramming	Low
HUTCHMED	Surufatinib	Preclinical	April 8th	9am	Poster	<u>2128</u>	2128. Surufatinib treatment in pancreatic cancer: unveiling the role of GPR34 in TAMs and enhancing immunotherapy efficacy	Low
HUTCHMED	Surufatinib	Preclinical	April 8th	9am	Poster	<u>2129</u>	2129. Efficacy and underlying mechanisms of surufatinib combined with PD-1 monoclonal antibody and chemotherapy in pancreatic cancer	Low
<b>April 9th (Monday)</b>								
Revolution Medicine	RMC-7977	Preclinical	April 9th	9am	Poster	<u>4709 / 2</u>	The RASMULTI(ON) inhibitor RMC-7977 blocks downstream MAPK and PI3K pathway activation in KRASG12X_mutant cancers	Low
Revolution Medicine	RMC-6236	Preclinical	April 9th	2:35pm	Oral	<u>6585</u>	Combination RASG12C(ON) and RASMULTI(ON) inhibition overcomes resistance and prolongs durability in preclinical models of mutant KRASG12C-driven cancers	Low
Xencor	xaluritamig	Preclinical	April 9th	1:30pm	Poster	<u>6348 / 9</u>	Unveiling diverse trimeric forms of STEAP1 in human prostate cancer cells: Exploring STEAP1-STEAP2 interdependence for expression and plasma membrane localization	Low
HUTCHMED	Fruquintinib	Preclinical	April 9th	1:30pm	Poster	<u>3827 / 17</u>	Optimizing the treatment schedule of radiotherapy combined with VEGFR-TKIs and PD-(L) 1 inhibitors in metastatic colorectal cancer	Low
HUTCHMED	Fruquintinib	Phase 3	April 9th	1:30pm	Poster	<u>6408 / 20</u>	Early carcinoembryonic antigen (CEA) dynamics to predict the efficacy of fruquintinib (F) + best supportive care (BSC) in patients with metastatic colorectal cancer (mCRC) enrolled in FRESCO-2	Low
HUTCHMED	Savolitinib	Phase 1/2	April 9th	1:30pm	Poster	<u>CT225 / 15</u>	CT251. Savolitinib (savo) + osimertinib (osi) vs savo + placebo (PBO) in patients (pts) with EGFR-mutated (EGFRm), MET-amplified advanced NSCLC with progression on osi	Medium
HUTCHMED	Surufatinib	Preclinical	April 9th	9am	Poster	<u>2122 / 13</u>	2122 / 13 - Enhanced anticancer efficacy via ROS-dependent ferroptosis: Synergy between surufatinib and cisplatin in small cell lung cancer	Low

**Exhibit 1: AACR 2024 Planner**

We summarize key presentations to watch for at AACR 2024

Company	Program	Stage	Day	Time (PST)	Type	Abstract No.	Titles	Importance
HUTCHMED	Surufatinib	Phase 2	April 9th	1:30pm	Poster	<u>CT266</u>	CT266. Initial efficacy of surufatinib plus sintilimab and IBI310 for patients with high-grade advanced-neuroendocrine neoplasm: A multicenter, single arm phase 2 study	Medium
<b>April 10th (Monday)</b>								
Krystal Biotech	KB-707	Preclinical	April 10th	9am	Poster	<u>7260 / 27</u>	An HSV-1-based vector for local delivery of IL-12 and IL-2 reshapes the immune landscape leading to tumor clearance and systemic immune surveillance	Low

Source: BofA Global Research

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**Exhibit 2: Stocks mentioned**

Rating and price summary

BofA Ticker	Bloomberg ticker	Company name	Price	Rating
HCM	HCM US	Hutchmed China Ltd	US\$ 13.83	C-1-9
KRYS	KRYS US	Krystal	US\$ 170.84	C-1-9
RVMD	RVMD US	Revolution Medicines	US\$ 29.94	C-1-9

Source: BofA Global Research

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**Price objective basis & risk****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 amdzalisib, \$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.

**Krystal Biotech (KRYS)**

Our \$200/share price objective is based on a probability-adjusted net present value (NPV) for rare dermatology (\$128/share), respiratory, including cystic fibrosis (CF) and AATD (\$9/share), aesthetics through the Jeune subsidiary (\$5/share), the discovery pipeline (\$36/share), and cash (\$21/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.

**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).

## 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
<b>BUY</b>				
	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
	Insmid Incorporated	INSM	INSM US	Jason Zemansky
	Intellia Therapeutics	NTLA	NTLA US	Greg Harrison, CFA
	Janux Therapeutics	JANX	JANX US	Alec W. Stranahan
	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
	Traverse 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
<b>NEUTRAL</b>				
	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	BMJ	BMJ 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
	Kymira Therapeutics	KYMR	KYMR US	Geoff Meacham
	Moderna	MRNA	MRNA US	Geoff Meacham
	Pfizer	PFE	PFE US	Geoff Meacham
	Recursion Pharmaceuticals, Inc.	RXR	RXR US	Alec W. Stranahan
	Tyra Biosciences	TYRA	TYRA US	Greg Harrison, CFA
	Vir	VIR	VIR US	Alec W. Stranahan
	Y-mAbs Therapeutics, Inc	YMAB	YMAB US	Alec W. Stranahan
<b>UNDERPERFORM</b>				
	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
	Novavax	NVAX	NVAX US	Alec W. Stranahan
	Regeneron Pharmaceuticals Inc.	REGN	REGN US	Geoff Meacham
	Reneo Pharmaceuticals	RPHM	RPHM US	Jason Zemansky
	TG Therapeutics	TGTX	TGTX US	Alec W. Stranahan
	United Therapeutics Corporation	UTHR	UTHR US	Greg Harrison, CFA

## Disclosures

## Important Disclosures

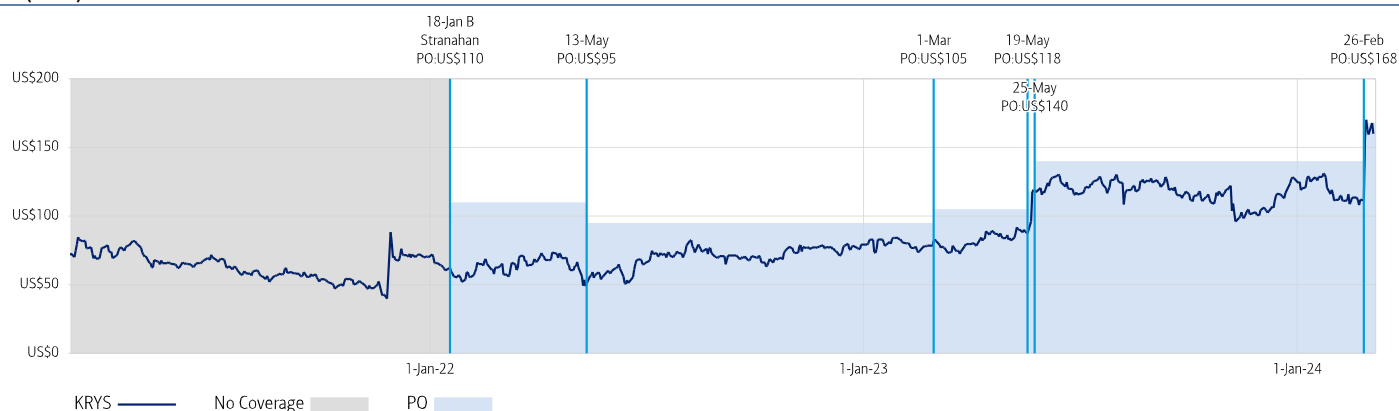
## Hutchmed China Ltd (HCM) Price Chart



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

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

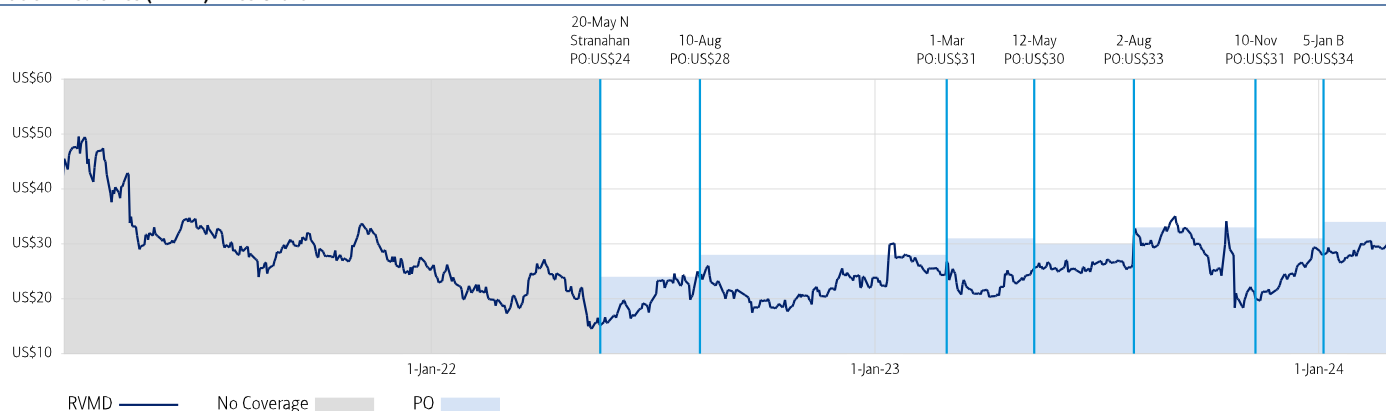
## Krystal (KRYS) Price Chart



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

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## Revolution Medicines (RVMD) Price Chart



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

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

Coverage Universe	Count	Percent	Inv. Banking Relationships <sup>R1</sup>	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 <sup>R1</sup>	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%

<sup>R1</sup> 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 <sup>R2</sup>
Buy	≥ 10%	≤ 70%
Neutral	≥ 0%	≤ 30%
Underperform	N/A	≥ 20%

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