Revolution Medicines Reports Fourth Quarter and Full Year 2022 Financial Results and Update on Corporate Progress

February 27, 2023

Early clinical data on RMC-6236 provided in support of RAS(ON) Inhibitor platform validation

Additional data releases for RMC-6236 (RAS^{MULTI}) and RMC-6291 ($KRAS^{G12C}$) expected in 2023

RMC-9805 ($KRAS^{G12D}$) expected to begin clinical development in mid-2023

Growing pipeline of development-stage assets, including RMC-0708 ($KRAS^{Q61H}$), that target every major RAS cancer mutation hotspot

Webcast today at 4:30 p.m. Eastern Time

REDWOOD CITY, Calif., Feb. 27, 2023 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing targeted therapies for RAS-addicted cancers, today announced its financial results for the quarter and year ended December 31, 2022, and provided an update on corporate progress.

"2022 saw the entry of our first two RAS(ON) Inhibitor candidates, RMC-6236 (RAS^{MULTI}) and RMC-6291 ($KRAS^{G12C}$), into clinical development," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. "For RMC-6236, initial pharmacokinetics, molecular, radiographic and tolerability/safety data provide encouraging evidence that we are dosing patients at clinically active and tolerated doses. Consistent with its preclinical profile, RMC-6236 has shown promising preliminary antitumor activity against multiple tumor types and genotypes. Combined with initial evidence of clinical activity for RMC-6291, we are encouraged that these data should have positive readthrough to our broad portfolio of RAS(ON) Inhibitors.

"In addition, IND-enabling development of RMC-9805, a mutant-selective RAS(ON) Inhibitor drug candidate designed to target cancers driven by the $KRAS^{G12D}$ mutation, is progressing toward first-in-human dosing mid-year. And we recently announced the advancement of RMC-0708, a mutant-selective inhibitor of the $KRAS^{Q61H}$ cancer variant, into IND-enabling development.

"As a result of the exceptional work of our entire organization, Revolution Medicines' portfolio now includes clinical and development-stage assets that may be applicable to the majority of RAS-addicted cancers, including compounds targeting every major RAS cancer mutation hotspot — G12, G13 and Q61. Early results from our first wave of RAS(ON) Inhibitors support continued investment in advancing our development pipeline of clinical and preclinical RAS(ON) Inhibitors and clinical RAS Companion Inhibitors. Building on this ongoing portfolio progress and encouraging signs, part of management's bandwidth is now directed toward defining the paths and steps we need to take now and over the next several years to ensure that we can maximize the value of these product candidates."

Clinical and Development Highlights

RAS(ON) Inhibitors

RMC-6236 (RAS^{MULTI})

RMC-6236 is an oral RAS(ON) Inhibitor designed to treat patients with cancers driven by a variety of RAS mutations, including $KRAS^{G12D}$, $KRAS^{G12V}$ and $KRAS^{G12R}$. Initially being evaluated as monotherapy, it may also be deployed as a RAS Companion Inhibitor in combination with mutant-selective RAS(ON) Inhibitors.

- The ongoing Phase 1/1b monotherapy trial (NCT05379985) is a multicenter, open-label, dose-escalation and dose-expansion study of RMC-6236 in patients with advanced solid tumors harboring select $KRAS^{G12}$ mutations, including $KRAS^{G12D}$, $KRAS^{G12V}$ and $KRAS^{G12R}$.

- Early findings have shown that RMC-6236 is orally bioavailable in patients, exhibiting pharmacokinetics consistent with our preclinical data and delivering dose-dependent increases in plasma exposure on once daily dosing and is generally well tolerated. A recommended phase 2 dose has not been established yet.

- 36 patients were evaluable for initial safety and tolerability in the study as of the data cut-off date of February 17, 2023. All of these patients had been previously treated with standard of care and/or other regimens, with an overall median of three prior treatments. As of this data cut-off, RMC-6236 was generally well tolerated in this group. Some patients have exhibited predicted and manageable on-target normal tissue effects.

- 12 patients — three non-small cell lung cancer (NSCLC) and nine pancreatic cancer —treated with RMC-6236 at doses o 40 mg, 80 mg or 120 mg daily were efficacy evaluable as of the February 17, 2023 data cut-off date. All 12 patients exhibited stable disease or better as their best response; 10 of these had reductions in tumor volume as of the data cut-off date. Importantly, as of the data cut-off date, all patients remained on study, with total duration of approximately 1.5-4.5 months. One patient with $KRAS^{G12D}$ NSCLC treated with 80 mg achieved a partial response (PR) on first re-staging scan that was subsequently confirmed by a follow-up scan. One patient with metastatic $KRAS^{G12D}$ pancreatic cancer who progressed following a third course of chemotherapy received RMC-6236 80 mg daily and has tolerated it well. At baseline the patient had three distinct lesions in the lung that are followed radiographically. At six weeks, all three tumor lesions

were reduced in size, reported as 17% reduction by Response Evaluation Criteria in Solid Tumors (RECIST). At 12 weeks, all three residual lesions were barely detectable, and the patient achieved a 70% reduction and PR by RECIST. The patient continues on study as of the data cut-off date and confirmation of the response awaits a follow-up scan.

- The company currently plans to provide further evidence of first-in-class single agent activity for RMC-6236 in mid-2023.

RMC-6291 ($KRAS^{G12C}$)

RMC-6291, an oral, selective, covalent inhibitor of $KRAS^{G12C}$(ON) designed to treat patients with cancers driven by the $KRAS^{G12C}$ mutant, is the first of the company's mutant-selective RAS(ON) Inhibitors to enter clinical development and the first publicly reported inhibitor of KRAS ^{G12C} that exhibits a highly differentiated mechanism of action.

- The ongoing Phase 1/1b monotherapy trial (NCT05462717) is a multicenter, open-label, dose-escalation and dose-expansion study of RMC-6291 in patients with advanced $KRAS^{G12C}$ mutant solid tumors. Early findings have shown that RMC-6291 is orally bioavailable and has exhibited pharmacokinetics consistent with preclinical findings and is generally well tolerated. A recommended phase 2 dose and schedule have not been established yet. Initial molecular and radiographic data indicate that the company is dosing RMC-6291 in a pharmacologically active range.

- The company currently plans to provide preliminary evidence of a superior profile for this compound in the second half of 2023.

RMC-9805 ($KRAS^{G12D}$)

RMC-9805 is an oral, selective, covalent inhibitor of $KRAS^{G12D}$(ON), the most common driver of RAS-addicted human cancers, predominantly among patients with pancreatic cancer, NSCLC or colorectal cancer (CRC). The company believes RMC-9805 is the first oral and covalent inhibitor of $KRAS^{G12D}$.

- The company currently expects to announce dosing of the first patient in a monotherapy dose-escalation study of RMC-9805 in mid-2023.

RAS Innovation Engine

Beyond this first wave of RAS(ON) Inhibitors, the company continues expanding its pipeline of RAS(ON) Inhibitor candidates.

- RMC-0708 is a potent, oral and selective non-covalent inhibitor of the $KRAS^{Q61H}$(ON) cancer variant. $KRAS^{Q61H}$ is found in approximately 10,000 new cancer cases in the U.S. each year divided evenly across lung cancer, CRC, pancreatic cancers and multiple myeloma. RMC-0708 is the company's first mutant-selective RAS(ON) inhibitor drug candidate to engage its RAS target non-covalently.

- RMC-8839 is a potent, oral and selective inhibitor of $KRAS^{G13C}$(ON). The company believes RMC-8839 is the first compound to directly inhibit $KRAS^{G13C}$, an important therapeutic target primarily for NSCLC and select CRC patients unserved by a targeted RAS inhibitor.

- The company continues drug discovery efforts in RAS(ON) Inhibitor pipeline expansion programs focused on RAS mutation hotspots including $KRAS^{G12R}$, $KRAS^{G12V}$, $KRAS^{G13D}$, RAS^{Q61X} and other important targets.

RAS Companion Inhibitors

RMC-4630 (SHP2)

RMC-4630 is a clinical-stage, oral inhibitor of SHP2, which contributes to tumor survival and growth in many RAS-addicted cancers.

RMC-4630 and $KRAS^{G12C}$ Inhibitor Lumakras™ (sotorasib)

- CodeBreaK 101c: Amgen has reported preliminary results from this Phase 1b trial evaluating the combination of RMC-4630 with the $KRAS^{G12C}$ inhibitor sotorasib in patients with advanced $KRAS^{G12C}$-mutated solid tumors. The results demonstrated that the combination was safe and tolerable, and showed promising early clinical activity in NSCLC patients with $KRAS^{G12C}$ mutations, particularly in patients who were $KRAS^{G12C}$ inhibitor-naïve.

- RMC-4630-03: Revolution Medicines continues conducting its global Phase 2 trial RMC-4630-03 (NCT05054725), a multicenter, open-label study of RMC-4630 in combination with sotorasib for patients with NSCLC with a $KRAS^{G12C}$ mutation who have failed prior standard therapy and who have not previously been treated with a $KRAS^{G12C}$ inhibitor. The company is conducting the trial in collaboration with Amgen, which is supplying sotorasib to trial sites globally. The study is fully enrolled and Revolution Medicines currently expects to provide topline data from this study in the second half of 2023.

- The company expects to evaluate RMC-4630 in combination with its RAS(ON) Inhibitors in the future.

Sanofi, Revolution Medicines' partner for the development of RMC-4630, provided notice of termination of their global SHP2 development and commercialization collaboration, effective as of June 2023. The companies are collaborating for the transition of all Sanofi's rights and obligations related to RMC-4630 back to Revolution Medicines over the first half of 2023. Following termination, Revolution Medicines will regain all global rights to RMC-4630.

RMC-5552 (mTORC1/4EPB1)

RMC-5552 is a first-in-class, bi-steric mTORC1-selective inhibitor designed to suppress phosphorylation and inactivation of 4EBP1 in cancers with hyperactive mTORC1 signaling, including certain RAS-addicted cancers. The company aims to combine RMC-5552 with RAS(ON) Inhibitors in patients with cancers harboring RAS/mTOR pathway co-mutations.

- Dose optimization continues in the company's ongoing multicenter, open-label, Phase 1/1b dose-escalation study evaluating RMC-5552 monotherapy in patients with refractory solid tumors (NCT04774952). As with RMC-4630, the company expects to evaluate RMC-5552 in combination with its RAS(ON) Inhibitors in the future.

- The company currently anticipates disclosing additional evidence of single agent activity for this compound in 2023.

Fourth Quarter and Full Year 2022 Financial Highlights

Cash Position: Cash, cash equivalents and marketable securities were $644.9 million as of December 31, 2022, compared to $577.1 million as of December 31, 2021. The increase was primarily attributable to the company's public equity offering in July 2022.

Revenue: Total revenue was $15.3 million for the quarter ended December 31, 2022, compared to $9.5 million for the quarter ended December 31, 2021 and consisted of revenue from the company's collaboration agreement on SHP2 inhibitors with Sanofi. During the quarter ended December 31, 2022, the company recorded a non-cash GAAP accounting adjustment that increased collaboration revenue by $7.6 million. This non-cash revenue adjustment was due to the termination of the Sanofi collaboration agreement which resulted in changes to the company's estimates of the accounting transaction price and estimated percentage of completion of work performed to date and resulted in a cumulative catch-up adjustment to collaboration revenue in the quarter.

Total revenue was $35.4 million for the year ended December 31, 2022, compared to $29.4 million for the year ended December 31, 2021. The increase in revenue was primarily due to the non-cash revenue adjustment.

R&D Expenses: Research and development expenses were $66.1 million for the quarter ended December 31, 2022, compared to $53.7 million for the quarter ended December 31, 2021. Research and development expenses were $253.1 million for the year ended December 31, 2022, compared to $186.9 million for the year ended December 31, 2021. The increases were primarily due to an increase in RMC-6236 and RMC-6291 expenses as a result of commencing clinical trials in 2022, an increase in personnel-related expenses related to additional headcount, an increase in research expenses associated with the company's pre-clinical research portfolio, and an increase in stock-based compensation.

G&A Expenses: General and administrative expenses were $10.9 million for the quarter ended December 31, 2022, compared to $8.7 million for the quarter ended December 31, 2021. General and administrative expenses were $40.6 million for the year ended December 31, 2022, compared to $30.5 million for the year ended December 31, 2021. The increases were primarily due to an increase in stock-based compensation and an increase in personnel-related expenses related to additional headcount.

Net Loss: Net loss was $56.5 million for the quarter ended December 31, 2022, compared to net loss of $52.7 million for the quarter ended December 31, 2021. Net loss was $248.7 million for the year ended December 31, 2022, compared to net loss of $187.1 million for the year ended December 31, 2021.

Financial Guidance

Revolution Medicines expects full year 2023 GAAP net loss to be between $335 and $365 million, which includes estimated non-cash stock-based compensation expense of $40 million and $50 million.

Based on the company's current operating plan, the company projects current cash, cash equivalents and investments can fund planned operations through 2024.

Webcast
Revolution Medicines will host a webcast this afternoon, February 27, 2023, at 4:30 p.m. Eastern Time (1:30 p.m. Pacific Time). To listen to the live webcast, or access the archived webcast, please visit: https://ir.revmed.com/events-and-presentations. Following the live webcast, a replay will be available on the company's website for at least 14 days.

About Revolution Medicines, Inc.
Revolution Medicines is a clinical-stage oncology company developing novel targeted therapies for RAS-addicted cancers. The company's R&D pipeline comprises RAS(ON) Inhibitors designed to suppress diverse oncogenic variants of RAS proteins, and RAS Companion Inhibitors for use in combination treatment strategies. The company's RAS(ON) Inhibitors RMC-6236 (RAS ^{MULTI}) and RMC-6291(KRAS^{G12C}) are currently in clinical development. Additional RAS(ON) Inhibitors in the company's pipeline include RMC-9805 (KRAS ^{G12D}) and RMC-0708 (KRAS^{Q61H}), both of which are currently in IND-enabling development, RMC-8839 (KRAS^{G13C}), and additional compounds targeting other RAS variants. RAS Companion Inhibitors in clinical development include RMC-4630 (SHP2) and RMC-5552 (mTORC1/4EBP1).

Lumakras™ (sotorasib) is a trademark of Amgen Inc.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Any statements in this press release that are not historical facts may be considered "forward-looking statements," including without limitation statements regarding the company's financial projections; the company's development plans and timelines and its ability to advance its portfolio and R&D pipeline; progression of clinical studies and findings from these studies, including the tolerability and potential efficacy of the company's candidates being studied; the potential advantages and effectiveness of the company's clinical and preclinical candidates, including its RAS(ON) Inhibitors; the ability of the company's product candidates to meet unmet medical needs and to be applicable to the majority of RAS-addicted cancers; whether data available from RMC-6236 and RMC-6291 will have positive readthrough to the company's portfolio of RAS(ON) Inhibitors; the company's ability to maximize the value of its product candidates; the potential of RMC-6236 to be first-in-class; the potential of RMC-6291 to show superior activity; the transition of rights and obligations related to RMC-4630 from Sanofi to the company; the potential of RMC-5552 to be first-in-class; the company's plans to study RMC-5552 in combination with RAS inhibitors and the company's aim to combine RMC-5552 with RAS(ON) Inhibitors in patients with cancers harboring RAS/mTOR pathway co-mutations. Forward-looking statements are typically, but not always, identified by the use of words such as "may," "will," "would," "believe," "intend," "plan," "anticipate," "estimate," "expect," and other similar terminology indicating future results. Such forward-looking statements are subject to substantial risks and uncertainties that could cause the company's development programs, future results, performance, or achievements to differ materially from those anticipated in the forward-looking statements. Such risks and uncertainties include without limitation risks and uncertainties inherent in the drug development process, including the company's programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with

manufacturing drug products, the company's ability to successfully establish, protect and defend its intellectual property, other matters that could affect the sufficiency of the company's capital resources to fund operations, reliance on third parties for manufacturing and development efforts, changes in the competitive landscape and the effects on the company's business of the COVID-19 pandemic and other global events. For a further description of the risks and uncertainties that could cause actual results to differ from those anticipated in these forward-looking statements, as well as risks relating to the business of Revolution Medicines in general, see Revolution Medicines' Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 27, 2023, and its future periodic reports to be filed with the Securities and Exchange Commission. Except as required by law, Revolution Medicines undertakes no obligation to update any forward-looking statements to reflect new information, events, or circumstances, or to reflect the occurrence of unanticipated events.

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REVOLUTION MEDICINES, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Revenue:				
Collaboration revenue	$ 15,330	$ 9,460	$ 35,380	$ 29,390
Total revenue	15,330	9,460	35,380	29,390
Operating expenses:				
Research and development	66,127	53,681	253,073	186,948
General and administrative	10,910	8,692	40,586	30,450
Total operating expenses	77,037	62,373	293,659	217,398
Loss from operations	(61,707)	(52,913)	(258,279)	(188,008)
Other income, net:				
Interest income	5,077	237	9,154	929
Interest and other expense	—	—	—	(12)
Total other income, net	5,077	237	9,154	917
Loss before income taxes	(56,630)	(52,676)	(249,125)	(187,091)
Benefit from income taxes	123	—	420	—
Net loss	$ (56,507)	$ (52,676)	$ (248,705)	$ (187,091)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.63)	$ (0.71)	$ (3.08)	$ (2.57)
Weighted-average common shares used to compute net loss per share, basic and diluted	89,158,785	73,831,121	80,626,525	72,806,079

REVOLUTION MEDICINES, INC.
SELECTED CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, unaudited)

	December 31, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$ 644,943	$ 577,054
Working capital (1)	598,201	529,423
Total assets	811,930	737,988
Deferred revenue	4,459	18,931
Total liabilities	126,742	135,420
Total stockholders' equity	685,188	602,568

(1) Working capital is defined as current assets less current liabilities.