Revolution Medicines Reports First Quarter Financial Results and Update on Corporate Progress

May 10, 2021

Multiple AACR Presentations Highlight Potential Advantages of RAS(ON) Inhibitors;
Scientific Publication is First to Demonstrate Anti-Drug Resistance Features

Continued Advancement and Enrollment of Multiple RMC-4630 RAS Companion Inhibitor Combination Studies; Initiated Clinical Evaluation of RMC-5552

Successfully Completed Financing Raising $281 Million in Net Proceeds

REDWOOD CITY, Calif., May 10, 2021 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage precision oncology company focused on developing targeted drugs to inhibit frontier targets that drive and sustain RAS-addicted cancers, today announced its financial results for the first quarter of 2021 and provided a corporate update.

"Revolution Medicines has made excellent progress reinforcing our belief that the company's cohesive portfolio of innovative clinical and preclinical assets will power compelling rational, mechanism-based combination treatments that provide benefit to patients with RAS-addicted cancers," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines.

"We presented data at the AACR Annual Meeting 2021 demonstrating the attractive preclinical profiles of two pioneering RAS(ON) inhibitor candidates that are currently undergoing IND-enabling development, RMC-6291 ($KRAS^{G12C}$) and RMC-6236 (RAS^{MULTI}). These first examples of RAS(ON) inhibitors intended for human use exhibit differentiated breadth, depth and durability of anti-tumor effects in human cancer models. Further, an important recent scientific paper described multiple genetic mutations causing clinical resistance to leading $KRAS^{G12C}$(OFF) inhibitors but with preserved sensitivity to RAS(ON) inhibitors from our collection. We believe that RMC-6291, RMC-6236 and additional emerging inhibitors in our portfolio hold great promise for use in treating, and overcoming resistance in, patients with a diverse range of RAS-addicted cancers lacking adequate targeted therapeutics.

"The company also continues broad-based initiatives with our RAS Companion Inhibitor portfolio. For RMC-4630 (SHP2), combination approaches with multiple direct RAS inhibitors remain a high-priority treatment strategy supported by the clinical and preclinical anti-tumor activity, resistance and safety data observed to date across these classes of targeted agents. Amgen's CodeBreaK 101c study evaluating the combination with sotorasib has demonstrated acceptable tolerability, has cleared early dose levels and is currently dosing patients at the target dose of RMC-4630 (200 mg on a Day 1/Day 2 weekly schedule). We also continue evaluating a second, distinct group of treatment strategies for RMC-4630 in combination with established drugs that potently suppress the RAS signaling pathway, including cobimetinib, a MEK inhibitor and osimertinib, an EGFR inhibitor, to determine whether enhanced pathway inhibition from these drug combinations delivers sufficient anti-tumor activity and tolerability to confer clinical benefit.

"We are also pleased to have begun clinical evaluation of RMC-5552 (mTORC1/4EBP1) in a monotherapy dose-escalation study. In aggregate, these projects with our RAS Companion Inhibitor portfolio, including continued IND-enabling development of RMC-5845 (SOS1), support our long-term goal of combining these assets with RAS(ON) Inhibitors on behalf of patients selected by molecular tumor features.

"To support the expanded and advancing pipeline, Revolution Medicines successfully completed a financing in the first quarter that helped position the company with a strong balance sheet."

R&D Highlights

RAS(ON) Inhibitors – Revolution Medicines continues maturing its first-in-class RAS(ON) Inhibitor platform, including an expansive collection of tri-complex inhibitors targeting diverse oncogenic RAS variants through highly differentiated chemical and pharmacologic profiles.

- **Potential advantages of RAS(ON) Inhibitors –** A recent paper in *Cancer Discovery* by Dr. Ryan Corcoran's team at the Massachusetts General Hospital/Harvard Medical School identified multiple resistance mutations that bypass the effects of three first-generation $KRAS^{G12C}$(OFF) inhibitors. Importantly, the researchers found that a $KRAS^{G12C}$-selective RAS(ON) tool compound from the Revolution Medicines portfolio, RM-018, retained potent binding and inhibitory activity against tumor cells harboring an on-target mutation that conferred resistance to all three $KRAS^{G12C}$(OFF) inhibitors tested.

- **RMC-6291 ($KRAS^{G12C}$)**
  - RMC-6291 is a first-in-class, potent, oral and selective tri-complex inhibitor of $KRAS^{G12C}$(ON) and $NRAS^{G12C}$(ON) with an attractive and differentiated preclinical profile designed to address persistent unmet needs for patients with cancers caused by $KRAS^{G12C}$ or $NRAS^{G12C}$.
  - Data presented at the American Association for Cancer Research (AACR) Annual Meeting 2021 showed superior anti-tumor activity for RMC-6291 in preclinical lung and colorectal cancer models driven by a $KRAS^{G12C}$ mutation.
  - The company remains on track to submit an investigational new drug (IND) application in the first half of 2022.

- **RMC-6236 (RAS^{MULTI})**
  - RMC-6236 is a first-in-class, potent, oral RAS-selective tri-complex, RAS^{MULTI}(ON) inhibitor with an attractive preclinical profile and is designed to treat cancers caused by multiple RAS variants for which no targeted treatment

is currently available.
- Data presented at the recent AACR meeting demonstrated deep anti-tumor activity of RMC-6236 in preclinical lung, colorectal and pancreatic cancer models driven by various mutations that are common drivers of human cancers, including $KRAS^{G12V}$ and $KRAS^{G12D}$.
- The company remains on track to submit an IND in the first half of 2022.

- **Continued expansion of other RAS(ON) inhibitor programs** – Revolution Medicines continues to progress an expanding portfolio of potent, cell-active RAS(ON) Inhibitors with the potential to target RAS variants driving the vast majority of RAS-addicted cancers. In particular, the company's $KRAS^{G12D}$- and $KRAS^{G13C}$-selective programs continue to advance in lead optimization. The company remains on track to nominate a third development candidate from its RAS(ON) inhibitor portfolio in the second half of 2021.

RAS Companion Inhibitors – Revolution Medicines continues to advance and expand multiple clinical studies both as monotherapy and in targeted drug combinations designed to achieve maximum clinical benefit.

- **RMC-4630 (SHP2 Inhibitor) –** RMC-4630 is a potent, oral, selective inhibitor of the SHP2 protein, a central node in the RAS signaling pathway. Its development is being advanced in partnership with, and is primarily funded by, Sanofi, both as monotherapy and in several current and planned combinations.

RMC-4630 and $KRAS^{G12C}$ inhibitor sotorasib

- To date, the available data from the ongoing Amgen-sponsored CodeBreaK 101c study of the RMC-4630 and sotorasib combination has demonstrated acceptable tolerability and cleared early dose levels.
- The CodeBreaK 101c study is currently dosing patients at the target dose of RMC-4630 (200 mg on a Day 1 / Day 2 weekly schedule, the full dose used by the company in monotherapy) in combination with sotorasib. The company looks forward to selection of a combination dose for this study in the second half of 2021.

RMC-4630 and AstraZeneca $KRAS^{G12C}$ inhibitor

- AstraZeneca plans to evaluate RMC-4630 in combination with an emerging asset targeting $KRAS^{G12C}$(OFF) from AstraZeneca's portfolio

RMC-4630 and MEK inhibitor cobimetinib (Cotellic®)

- Phase 1b/2 study of this combination is ongoing, including in expansion cohorts of patients with $KRAS^{MUTANT}$ colorectal cancer at the recommended Phase 2 dose and schedule (RP2DS) for this combination. The company continues to expect preliminary safety and clinical activity data from this expansion study in 2022.

RMC-4630 and EGFR inhibitor osimertinib (Tagrisso®)

- Dosing and enrollment continue in the Phase 1b study of this combination and the company continues to expect initial tolerability and pharmacokinetic (PK) data in the second half of 2021.

RMC-4630 and PD-1 inhibitor pembrolizumab (Keytruda®)

- Sanofi-sponsored Phase 1 study of this combination continues. The RP2DS for this combination is expected in the first half of 2021 and expansion cohorts evaluating this combination in patients with non-small cell lung cancer (NSCLC) are planned.

RMC-4630 monotherapy

- Presented dose escalation activity data set from the ongoing Phase 1 study at the recent AACR meeting, showing anti-tumor activity and safety and tolerability that is consistent with on-pathway inhibition, delivering on a corporate milestone.
- Data presented at AACR meeting showed reduction of variant allele frequency in circulating tumor DNA (ctDNA) samples from patients treated with RMC-4630 for cancers carrying $KRAS^{G12C}$ or $NF1^{LOF}$, further validating the expected clinical mechanism of action of RMC-4630.

- **RMC-5552 (mTORC1/4EBP1 Inhibitor) –** RMC-5552 is a potent, selective bi-steric inhibitor of mTORC1 that suppresses phosphorylation and inactivation of 4EBP1.

    - Dosing and enrollment are underway in the recently initiated Phase 1 monotherapy dose-escalation study, delivering on a corporate milestone. The company continues to expect initial safety, PK and single agent activity data in 2022.
    - Preclinical data presented at the recent AACR meeting demonstrated that bi-steric mTORC1-selective inhibitors drive significant anti-tumor activity as monotherapy and in combination with $KRAS^{G12C}$ inhibitors in genetically-defined preclinical models of human cancers.
    - The company intends to evaluate RMC-5552 in combination with RAS inhibitors for the treatment of tumors driven

by co-occurring RAS mutations and genomic activation of the mTORC1 pathway.

- **RMC-5845 (SOS1 Inhibitor)** – RMC-5845 is a potent, selective, oral inhibitor of SOS1, a major switch in the cycling of RAS(OFF) to RAS(ON).
    - The company remains on track to submit an IND in the second half of 2021 to enable an initial monotherapy dose escalation study and intends to evaluate RMC-5845 for treatment of certain genetically defined RAS-dependent cancers.

Corporate Highlights

- **Completed upsized financing to strengthen balance sheet and support advancement of expanding pipeline –** Public offering of common stock in February 2021 raised net proceeds of $281 million, enabling the company to advance its pipeline, including RAS(ON) Inhibitors RMC-6291 and RMC-6236, through early Phase 1 signal-seeking clinical studies.

- **Flavia Borellini, Ph.D. joins existing board members Elizabeth McKee Anderson and Neil Exter as Class I director nominee –** Dr. Borellini has more than 25 years of executive management experience in the pharmaceutical and biotechnology industry, with a particular focus on global development of targeted oncology drugs, from preclinical to commercial stage.

First Quarter 2021 Financial Highlights

Cash Position: Cash, cash equivalents and marketable securities were $681.6 million as of March 31, 2021, compared to $440.7 million as of December 31, 2020. The increase was primarily due to proceeds from the company's equity public offering in February 2021.

Revenue: Total revenue, consisting of revenue from the company's collaboration agreement with Sanofi, was $10.1 million for the quarter ended March 31, 2021, compared to $11.5 million for the quarter ended March 31, 2020. The decrease was due to lower reimbursed research and development services for RMC-4630 resulting from lower manufacturing costs.

R&D Expenses: Research and development expenses were $40.9 million for the quarter ended March 31, 2021, compared to $27.5 million for the quarter ended March 31, 2020. The increase was primarily due to an increase in research expenses associated with the company's pre-clinical research portfolio, an increase in personnel-related expenses related to additional headcount, and an increase in stock-based compensation.

G&A Expenses: General and administrative expenses were $6.7 million for the quarter ended March 31, 2021, compared to $5.2 million for the quarter ended March 31, 2020. The increase was primarily due to an increase in personnel-related expenses related to additional headcount, and an increase in stock-based compensation.

Net Loss: Net loss was $37.2 million for the quarter ended March 31, 2021, compared to net loss of $19.5 million for the quarter ended March 31, 2020.

2021 Financial Guidance

Revolution Medicines continues to expect full year 2021 GAAP net loss to be between $170 million and $190 million, which includes estimated non-cash stock-based compensation expense of $20 million to $25 million.

About Revolution Medicines, Inc.

Revolution Medicines is a clinical-stage precision oncology company focused on developing novel targeted therapies to inhibit high-value frontier targets in RAS-addicted cancers. The company possesses sophisticated structure-based drug discovery capabilities built upon deep chemical biology and cancer pharmacology know-how and innovative, proprietary technologies that enable the creation of small molecules tailored to unconventional binding sites.

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. RAS(ON) Inhibitors in development include RMC-6291, RMC-6236, and a pipeline of research compounds targeting additional RAS variants. RAS Companion Inhibitors in development include RMC-4630, RMC-5552, and RMC-5845.

Keytruda® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Tagrisso® is a registered trademark of the AstraZeneca group of companies. Cotellic® is a registered trademark of Genentech, Inc. (a member of the Roche Group).

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 development plans and timelines and its ability to advance its portfolio and R&D pipeline; the company's belief that its assets will power compelling rational, mechanism-based combination treatments that provide benefit to patients with RAS-addicted cancers; dosing and enrollment in the company's clinical trials and the tolerability and potential efficacy of the company's candidates being studied; the ability of the company's therapies to inhibit frontier targets in RAS-addicted cancers; the company's plans to advance the IND-enabling development of RMC-6291, RMC-6236 and RMC-5845; results from the company's single-agent and combination studies of RMC-4630; the company's plans to study RMC-5552 in combination with RAS inhibitors; the expected timing of results from the company's Phase 1 study of RMC-5552; the potential advantages and effectiveness of the company's preclinical candidates, including its RAS(ON) Inhibitors; the company's plans to nominate a third development candidate from its RAS(ON) inhibitor portfolio; and the company's plans to release data related to its RAS Companion Inhibitors. 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 our 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 our business of the worldwide COVID-19 pandemic. 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' Quarterly Report on Form 10Q filed with the Securities and Exchange Commission on May 10, 2021, 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.

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

	Three Months Ended March 31,	
	2021	**2020**
Revenue:		
Collaboration revenue	$ 10,131	$ 11,546
Total revenue	10,131	11,546
Operating expenses:		
Research and development	40,858	27,457
General and administrative	6,670	5,171
Total operating expenses	47,528	32,628
Loss from operations	(37,397)	(21,082)
Other income (expense), net:		
Interest income	233	909
Interest expense	(12)	(21)
Total other income (expense), net	221	888
Loss before income taxes	(37,176)	(20,194)
Benefit from income taxes	—	675
Net loss	$ (37,176)	$ (19,519)
Redeemable convertible preferred stock dividends - undeclared and cumulative	—	(2,219)
Net loss attributable to common stockholders	$ (37,176)	$ (21,738)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.53)	$ (0.74)
Weighted-average common shares used to compute net loss per share, basic and diluted	70,420,076	29,297,698

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

	March 31,	December 31,
	2021	**2020**
Cash, cash equivalents and marketable securities	$ 681,593	$ 440,741
Working capital (1)	653,646	406,946
Total assets	811,651	567,401
Deferred revenue	18,099	20,592
Total liabilities	89,071	92,725
Total stockholders' equity (deficit)	722,580	474,676

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

Contacts: For Investors: Vida Strategic Partners Stephanie Diaz 415-675-7401 sdiaz@vidasp.com For Media: Vida Strategic Partners Tim Brons 415-675-7402 tbrons@vidasp.com