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

August 11, 2021

Company Shows Continued Progress Demonstrating Differentiation of RAS(ON) Inhibitors, Targeting Additional RAS Variants and Progressing Assets Toward the Clinic

Initial Results of RMC-4630-02 Study Support Deprioritizing Certain Approaches and Focusing on Combinations of RMC-4630 with Direct RAS Inhibitors

New Amgen Clinical Collaboration and Supply Agreement for Planned Global Phase 2 Study, RMC-4630-03, Evaluating RMC-4630 in Combination with Lumakras ™

REDWOOD CITY, Calif., Aug. 11, 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 second quarter and six months ended June 30, 2021, and provided a corporate update.

"Treatment for RAS-addicted cancers reached an important milestone in the second quarter with the first FDA approval of a targeted medicine for lung cancer carrying the $KRAS^{G12C}$ mutation, Amgen's Lumakras™, or sotorasib. Likewise, Revolution Medicines continued making excellent progress reinforcing our belief that our cohesive and innovative asset portfolio can lead to rational, mechanism-based and beneficial combination treatments for patients. We have made the decision to deprioritize indirect combination treatment strategies represented in the RMC-4630-02 study while expanding evaluation of combination regimens with direct inhibitors of RAS proteins combined with our SHP2 inhibitor, RMC-4630. We are particularly gratified to conduct the RMC-4630-03 study under a clinical trial collaboration and supply agreement with Amgen through which we will evaluate the combination for potential additional benefit to lung cancer patients with the $KRAS^{G12C}$ tumor mutation. We also maintain strong momentum toward bringing our highly differentiated RAS(ON) Inhibitors to bear against a wide range of RAS-addicted cancers," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines.

R&D Highlights

RAS(ON) Inhibitors – Revolution Medicines continues to advance 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.

- **RMC-6291 ($KRAS^{G12C}$) -** RMC-6291 is a first-in-class, potent, oral and selective tri-complex inhibitor of $KRAS^{G12C}$(ON) with a differentiated preclinical profile designed to address persistent unmet needs for patients with cancers caused by $KRAS^{G12C}$.
  - During the second quarter, the company reported additional data at the American Association for Cancer Research (AACR) annual meeting and in a subsequent presentation showing that RMC-6291 provides deeper and/or more sustained anti-tumor effects in xenograft $KRAS^{G12C}$ cancer models compared to a first-generation RAS(OFF) inhibitor, expanding the evidence that RMC-6291 has the potential to be a best-in-class $KRAS^{G12C}$ inhibitor.
  - The company has expanded on initial results published in *Cancer Discovery* by Dr. Ryan Corcoran's team at the Massachusetts General Hospital/Harvard Medical School by demonstrating that RMC-6291 is active against all second-site resistance mutations reported thus far from patients treated with adagrasib. As many of these mutations also confer resistance to sotorasib and other $KRAS^{G12C}$(OFF) inhibitors, the activity of RMC-6291 in this setting illustrates a distinguishing property of the molecule that may be useful for preventing, or treating, emergence of these resistance mutations.
  - The company remains on track to submit an Investigational New Drug (IND) application for RMC-6291 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 that is designed to treat cancers caused by multiple RAS variants for which no targeted treatment is currently available.
  - During the second quarter, the company reported deep anti-tumor activity of RMC-6236 in preclinical lung, colorectal and pancreatic cancer models driven by various common mutations, including $KRAS^{G12V}$ and $KRAS^{G12D}$, at the AACR annual meeting and in a subsequent presentation, supporting its potential as a first targeted therapy for treating $KRAS^{G12V}$ and/or $KRAS^{G12D}$ tumors.
  - A study published by the Dana-Farber Cancer Institute in the *New England Journal of Medicine* identified "RAS oncogene switch" resistance mutations in patients treated with adagrasib. The company subsequently presented preclinical data demonstrating that RMC-6236 is active against all of these clinically observed variants, revealing important properties of RMC-6236 that may be useful for preventing, or treating, emergence of such resistance mutations.
  - The company remains on track to submit an IND for RMC-6236 in the first half of 2022.

- **Continued expansion of other RAS(ON) inhibitor programs** – Revolution Medicines continues to progress its expanding

portfolio of RAS(ON) Inhibitors designed to target RAS variants driving the vast majority of RAS-addicted cancers and 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 of its RAS Companion Inhibitors designed to provide maximum clinical benefit in RAS-addicted cancers.

- **RMC-4630 (SHP2 Inhibitor) –** RMC-4630 a potent, oral, selective inhibitor of the SHP2 protein, is being advanced in collaboration with, and is primarily funded by, Sanofi.

  - **RMC-4630 and KRAS^{G12C} inhibitor sotorasib**
    - Amgen's CodeBreaK 101c study continues evaluating sotorasib in combination with RMC-4630 in patients receiving second line or later treatment for advanced non-small cell lung cancer (NSCLC), colorectal cancer (CRC), and other solid tumors. To date this combination has demonstrated acceptable tolerability and cleared early dose levels. The dose escalation work continues at the target dose for each compound: RMC-4630 200 mg on a Day 1 / Day 2 (D1D2) weekly schedule, in combination with sotorasib 960 mg daily. Amgen anticipates selecting a combination dose for this study in the second half of 2021.
    - Today, Revolution Medicines announces a global Phase 2 study that will evaluate further the combination of RMC-4630 and sotorasib in lung cancer. The protocol for the new study, RMC-4630-03, is informed by the CodeBreaK 101c work to date as well as the many important learnings in the field over the last few years. The study, sponsored by Revolution Medicines under its global partnership with Sanofi, will be conducted in collaboration with Amgen, including supply of drug by Amgen at ex-U.S sites. RMC-4630-03 will evaluate the combination in inhibitor-naïve patients with advanced NSCLC that builds on, and is complementary to, CodeBreaK 101c. Study startup activities are ongoing, and the company expects to dose the first patient in the second half of 2021 and to have preliminary findings in the second half of 2022.

  - **RMC-4630 and MEK inhibitor cobimetinib (Cotellic®)**
    - Previously reported findings from the Phase 1b/2 study of this combination in patients with relapsed/refractory solid tumors harboring specific genomic mutations demonstrated acceptable tolerability, also observed among patients enrolled in expansion cohorts. Among 11 efficacy evaluable patients with NSCLC, one patient with a KRAS^{G12V} tumor mutation and gene amplification exhibited a confirmed partial response (PR) with a 45% tumor volume reduction. Among 25 efficacy evaluable CRC subjects, the best clinical response was stable disease. These results support the anti-tumor activity of RMC-4630 and its potential for clinical benefit in RAS-driven cancers and to be combined tolerably with other drugs. However, insufficient clinical benefit was observed to justify advancing this approach, and no additional patients will be enrolled in this study. The findings reinforce the company's belief that the optimal treatment for RAS-addicted cancers may come from combining RMC-4630 with direct RAS inhibitors.

  - **RMC-4630 and EGFR inhibitor osimertinib (Tagrisso®)**
    - The company initiated a Phase 1b study of this combination with the intent of suppressing adaptive resistance mechanisms that may eventually reduce the efficacy of osimertinib upon long-term treatment. To date, the company has not identified a combination dose and schedule with acceptable tolerability, indicating that the combined suppression of RAS signaling in normal tissues caused by these two agents presents too significant a safety hurdle to justify advancing this approach, and no further patients will be enrolled in this study. No clinical toxicity was observed that has been attributed to off-target effects of RMC-4630. Rather the company believes that osimertinib and RMC-4630 are both effective, and additive, on-pathway inhibitors. The company intends to increase its focus on RAS-addicted cancers by combining direct RAS inhibitors with RAS Companion Inhibitors including RMC-4630.

  - **RMC-4630 and PD-1 inhibitor pembrolizumab (Keytruda®)**
    - The TCD16210 study sponsored by Sanofi continues evaluating RMC-4630 in combination with pembrolizumab, a PD-1 inhibitor. Today, the company reports that preparation is underway for Phase 2 expansion focused on evaluating this combination as front-line treatment for patients with PD-L1+ NSCLC.

  - **RMC-4630 monotherapy**
    - The company presented a dose escalation activity data set from its ongoing Phase 1 study at the 2021 AACR annual meeting, showing anti-tumor activity and safety and tolerability that are consistent with on-pathway inhibition.
    - Additional data were presented at the AACR meeting showing reduction of variant allele frequency in circulating tumor DNA (ctDNA) samples from select patients treated with RMC-4630, further validating its expected clinical mechanism of action.

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

  - Enrollment and dosing are underway in a Phase 1 monotherapy dose-escalation study. The company continues to expect initial safety, pharmacokinetic and single agent activity data in 2022.

- The company reported preclinical data at the 2021 AACR annual meeting demonstrating that bi-steric mTORC1-selective inhibitors drive significant anti-tumor activity as monotherapy and in combination with $KRAS^{G12C}$ inhibitors in genetically-defined models of human cancers.
- The company recently announced the publication of an original scientific paper in *Nature Chemical Biology* describing anti-tumor effects of bi-steric mTORC1-selective inhibitors that potently suppress phosphorylation of 4EBP1, a key translational regulator of oncogene expression. In preclinical models, a series of bi-steric inhibitors demonstrated the favorable anti-tumor effects and tolerability of such compounds compared to earlier generations of mTOR inhibitors.
- 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 expects RMC-5845 to be IND-ready in the second half of 2021. Due to its current focus on other priorities, including the continued advancement of its RAS(ON) Inhibitor programs and the initiation of the RMC-4630-03 study, the company no longer intends to submit an IND for RMC-5845 in 2021 and will determine timing for a potential IND at a future date.

Corporate Highlights

- **Flavia Borellini, Ph.D. elected to board of directors –** 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.

Second Quarter 2021 Financial Highlights

Cash Position: Cash, cash equivalents and marketable securities were $646.3 million as of June 30, 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 $8.7 million for the quarter ended June 30, 2021, compared to $10.0 million for the quarter ended June 30, 2020. The decrease was due to lower reimbursed research and development services for RMC-4630 resulting from lower clinical trial costs.

R&D Expenses: Research and development expenses were $45.9 million for the quarter ended June 30, 2021, compared to $32.9 million for the quarter ended June 30, 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 $7.3 million for the quarter ended June 30, 2021, compared to $5.1 million for the quarter ended June 30, 2020. The increase was primarily due to stock-based compensation and personnel-related expenses related to additional headcount.

Net Loss: Net loss was $44.3 million for the quarter ended June 30, 2021, compared to a net loss of $27.2 million for the quarter ended June 30, 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 approximately $20 million.

Conference Call

Revolution Medicines will host a conference call and webcast this afternoon, August 11, 2021, at 4:30 PM EDT (1:30 PM PDT).

To listen to the conference call, please dial (833) 423-0425 or (918) 922-3069, provide conference ID: 9829729 and request the Revolution Medicines conference call. 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 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.

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 asset portfolio can lead to rational, mechanism-based and beneficial combination treatments for patients; dosing, expansion 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, including bringing its RAS(ON) inhibitors to bear against RAS-addicted cancers; the company's plans to submit an IND for RMC-6291 and RMC-6236; the company's plans to nominate a third development candidate from its RAS(ON) inhibitor portfolio; the selection of a combination dose for the CodeBreak 101c study; enrollment in and findings from the company's planned RMC-4630-03 study; the company's plans to study its RAS Companion Inhibitors, including RMC-4630 and RMC-5552, in combination with RAS inhibitors; the potential advantages and effectiveness of the company's preclinical candidates, including its RAS(ON) Inhibitors; the company's plans to release data related to its RAS Companion Inhibitors, including RMC-5552, and the related timing; and the company's expected net loss and estimated stock-based compensation expenses for the year ending December 31, 2021. 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 10-Q filed with the Securities and Exchange Commission on August 11, 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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Revenue:				
Collaboration revenue	$ 8,698	$ 10,025	$ 18,829	$ 21,571
Total revenue	8,698	10,025	18,829	21,571
Operating expenses:				
Research and development	45,936	32,918	86,794	60,375
General and administrative	7,297	5,091	13,967	10,262
Total operating expenses	53,233	38,009	100,761	70,637
Loss from operations	(44,535)	(27,984)	(81,932)	(49,066)
Other income (expense), net:				
Interest income	236	730	469	1,639
Interest expense	—	(19)	(12)	(40)
Total other income (expense), net	236	711	457	1,599
Loss before income taxes	(44,299)	(27,273)	(81,475)	(47,467)
Benefit from income taxes	—	58	—	733
Net loss	$ (44,299)	$ (27,215)	$ (81,475)	$ (46,734)
Redeemable convertible preferred stock dividends - undeclared and cumulative	—	—		(2,219)
Net loss attributable to common stockholders	$ (44,299)	$ (27,215)	$ (81,475)	$ (48,953)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.60)	$ (0.46)	$ (1.13)	$ (1.11)
Weighted-average common shares used to compute net loss per share, basic and diluted	73,399,714	58,752,494	71,917,508	44,025,372

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

	June 30, 2021	December 31, 2020
Cash, cash equivalents and marketable securities	$ 646,322	$ 440,741
Working capital (1)	615,210	406,946
Total assets	774,046	567,401
Deferred revenue	15,928	20,592
Total liabilities	89,040	92,725
Total stockholders' equity	685,006	474,676

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

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