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Repare Gets Cash And Validation In DNA Damage Repair Alliance With Roche

by Joseph Haas

Roche is paying $125m upfront to in-license potential blockbuster lead candidate camonsertib from Repare, which calls it a best-in-class ATR inhibitor and has the chance to opt back in on US commercialization.

Repare Therapeutics, Inc. got ample upfront cash, significant earnout potential, the chance to opt back in on US commercialization and, according to analysts, strong validation for its DNA damage repair (DDR) approach to cancer by licensing its lead candidate camonsertib (RP-3500) to Roche on 1 June.

The pharma is paying Repare $125m up front and up to $1.2bn in milestones in return for the asset, now in Phase I/II development for solid tumors.

Repare execs told a 1 June investor call that Roche is the ideal partner to take camonsertib forward as a monotherapy and potentially combined with other drugs across a variety of cancer types. In April, the biotech presented data from the ongoing Phase I/II TRESR study at an American Association for Clinical Research meeting that it asserted indicates a best-in-class profile for camonsertib in the ATR (Ataxia-Telangiectasia and RAD-3-related protein kinase) inhibitor class.

Data from the study were particularly promising in ovarian cancer, showing what Segal termed early clinical proof-of-concept with a 25% overall response rate, a 75% clinical benefit rate and median progression-free survival of 35 weeks in heavily pre-treated patients. Notably, 90% of ovarian cancer patients in the study had previously failed treatment with a PARP inhibitor and/or chemotherapy, the Cambridge, MA/Montreal-based firm said.

“Camonsertib is an oral ATR inhibitor designed to treat cancers with DNA damage response (DDR) defects, and high replication stress,” Segal told the 1 June call. “This was our first clinical-

stage asset as a company when it entered the clinic in July 2020. ATR is a critical DNA damage response protein and it plays a central role in the regulation of cell replication stress."

Repare debuted in 2017 with $68m in series A funding from Versant Ventures and MPM Capital and a goal of bringing synthetic lethality candidates into the clinic by 2019. (Also see "*Versant & MPM Back Synthetic Lethality Newco With $68M*" - Scrip, 22 Jun, 2017.)

Multiple Cancer Players Focused On ATR Inhibition

Although no ATR inhibitors have reached Phase III yet, it is a busy class involving major names in cancer. According to Biomedtracker, *AstraZeneca PLC* has AZD6738 in Phase II in leukemia, lymphoma, breast cancer and other solid tumors; *Merck KGaA* has M6620 in Phase II for bladder, ovarian and lung cancer; and *Artios Pharma Limited* has ART0380 in Phase I/II in solid tumors. (Also see "*Artios Banks $153m On The Back Of Novartis And Merck KGaA Deals*" - Scrip, 30 Jul, 2021.) Another notable entry in the field is *Bayer AG*'s Phase I elimusertib (BAY 1895344), which showed minimal efficacy at toxic doses in data presented this year at AACR, noted Guggenheim analyst Charles Zhu. Those data bolstered Repare's case for best-in-class status for camonsertib, he added in a 1 June note.

The Repare/Roche alliance follows a March deal between *Bristol Myers Squibb Company* and *Volastra Therapeutics, Inc.*, in which the latter firm got $30m up front and could realize more than $1bn for investigating cancer targets with its synthetic lethality CINtech platform. (Also see "*BMS Is Latest To Join Synthetic Lethality Bandwagon With Volastra Deal*" - Scrip, 21 Mar, 2022.)

Segal said Repare is testing camonsertib in combination with PARP inhibitors and chemotherapy and thinks combinations with radiotherapy, immunotherapy and other DDR candidates, including its own Phase I PKMYT1 inhibitor RP-6306, a first-in-class agent, are also worth investigating. While Roche now assumes all clinical development responsibility for camonsertib, Repare retains a right to do its own combination testing of the ATR inhibitor with RP-6306, which is slated for a Phase I read-out early in the second half of 2022.

"The scale and scope of both monotherapy and combination opportunities underpinned our view that the best strategy to win in ATR inhibition for patients, for our team and for our shareholders was to partner with a best-in-class, proven leader in oncology, drug development and commercialization, preferably one with a global footprint and a commitment to precision oncology," Segal said. "We believe Roche has ticked all these boxes and more."

Roche is paying $125m up front for the candidate, with potential for up to $1.2bn in clinical, regulatory, commercial and sales milestones, of which $55m could be earned in the near term, Repare said. The biotech could also realize mid-single-digit to mid-teen global sales royalties if camonsertib reaches market. Further, Repare can opt into a US co-development and profit-sharing arrangement, participating in US promotion of the drug, while still qualifying for some of

the milestones and ex-US sales royalties.

Analysts See Camonsertib As Undervalued Asset

Guggenheim analyst Zhu said the deal represents "a best-case scenario for Repare, given compelling deal economics, and is deeply validating for Repare's platform." Investors have had lukewarm sentiment at times, the analyst said, adding that investors' view of the drug has often been misaligned compared to the relative excitement among clinicians."

But shareholders responded enthusiastically to the deal, as Repare's stock finished the trading day on 2 June up 45% to $12.67 per share.

Bloom Burton & Co. analyst David Martin agreed in a 2 June note that the deal validates both the drug, which he sees as having a "class-leading profile," and Repare's science.

"While this is not the largest single-asset biopharma license deal we have seen over the past 18 months ... it beats the sector average for upfront payment ($78.5m) and total deal size ($780m)," Martin noted.

Repare head of business and corporate development Kim Seth told the call the deal with Roche marks "a meaningful value-enhancing milestone" for the company, and extends its financial runway roughly two years into 2026. The company chose Roche as its partner after "an extensive partnering process to identify the best global partner for camonsertib," he added.

Repare raised a $235m initial public offering in 2020, which it supplemented with a $95m follow-on offering last October. (Also see "*Finance Watch: 2021 Is Now Two Away From 100 Biopharma IPOs*" - Scrip, 31 Oct, 2021.) The tie-up with Roche is Repare's third major deal, following a January 2019 agreement with Japan's *Ono Pharmaceutical Company, Ltd.* conferring Asian rights (except for mainland China) to its preclinical DNA polymerase theta inhibitor program (Also see "*Deal Watch: Xencor Adds New Bispecific Partner In Agreement With Genentech*" - Scrip, 6 Feb, 2019.) and a multi-target discovery collaboration signed with BMS in June 2020 focused on novel synthetic lethality targets for oncology. (Also see "*Deal Watch: Chinook To Go Public Via Reverse Merger With Troubled Aduro*" - Scrip, 2 Jun, 2020.)

Both of those partnered programs currently are in the discovery stage, according to Repare.