Molecular Partners Reports H1 2024 Corporate Highlights and Financials

August 26, 2024

First Radio-DARPin Therapy (RDT) candidate MP0712 nominated; supporting preclinical package presented at SNMMI; initial clinical data expected in 2025

Strategic collaboration agreement signed with Orano Med to co-develop ^{212}Pb-based RDT candidates for multiple oncology targets, including MP0712

MP0533 phase 1 dose escalation continues with cohort 8 open; clinical data update on amended dosing scheme expected in 2025

Switch-DARPin Platform: preclinical data supporting mechanism of action of Switch-DARPin concept and of first candidate MP0621 presented at EHA

MP0317 positive data of the completed Phase 1 trial presented at ASCO, confirming tumor microenvironment remodeling, favorable safety profile and dosing flexibility

Outlook: Funded into 2027 with cash and short-term deposits of CHF 159 million as of June 30, 2024, Molecular Partners expects total operating expenses of CHF 65 - 75 million in 2024

ZURICH-SCHLIEREN, Switzerland and CONCORD, Mass., Aug. 26, 2024 (GLOBE NEWSWIRE) -- **Ad hoc announcement pursuant to Art. 53 LR:** Molecular Partners AG (SIX: MOLN; NASDAQ: MOLN), a clinical-stage biotech company developing a new class of custom-built protein drugs known as DARPin therapeutics ("Molecular Partners" or the "Company"), today announced corporate highlights and unaudited financial results for the first half-year of 2024.

“In the first half of 2024, we made substantial progress with our Radio-DARPin Therapy (RDT) platform. We nominated the first RDT candidate, MP0712 targeting DLL3, and we look forward to bringing it to patients in 2025 with our partner Orano Med, the leader in the ^{212}Pb field. With them, we entered into a strategic collaboration earlier this year, to access and leverage their supply and manufacturing capabilities, as well as clinical experience, with radiopharmaceuticals, to co-develop Radio-DARPin Therapeutics together,” said Patrick Amstutz, Ph.D., Molecular Partners’ Chief Executive Officer. “Additionally, we progressed our immune cell engagers, including the cKit Switch-DARPin MP0621 into pre-clinical studies, and progressed MP0533 in AML to the top planned dose, seeing initial clinical responses and now testing dose intensification.”

Research & Development Highlights

Radio-DARPin Therapy (RDT) Platform and MP0712
Molecular Partners has leveraged the intrinsic properties of DARPins, such as small size, high affinity and specificity, to engineer Radio-DARPins as ideal vector candidates for radiopharmaceutical therapeutics and to create a Radio-DARPin Therapy (RDT) platform amenable to a broad range of tumor targets. Historically, small protein-based vectors faced challenges with kidney accumulation and toxicity, as well as suboptimal tumor uptake. Molecular Partners’ RDT platform addresses these limitations with its half-life extension technologies and surface engineering approaches, while preserving the advantages of the small protein format.

Throughout H1 2024, Molecular Partners has continued to demonstrate the RDT platform's ability to deliver on its intended design. The Company has engaged with scientific experts in radiopharmaceutical innovation, as well as investor and clinical communities to build awareness of the unique offering of Radio-DARPins and to identify opportunities for potential RDT portfolio growth.

In January 2024, Molecular Partners entered into a strategic collaboration with Orano Med to co-develop ^{212}Pb-based RDTs for patients with solid tumors. The partnership combines Molecular Partners' leadership in DARPins, as a highly differentiated modality for tumor-targeted delivery of radioisotopes, with Orano Med’s leading expertise and capabilities in Targeted Alpha Therapy to further advance the RDT platform and expand Molecular Partners’ RDT portfolio. ^{212}Pb represents the next generation of targeted alpha therapies, with a selective, safe, and potent profile in patients: in addition to virtually endless supply of starting material, Orano Med has established robust and independent supply and manufacturing capabilities required for seamless delivery of targeted alpha therapies to clinical sites.

In June 2024, Molecular Partners nominated MP0712 as its first RDT candidate, a ^{212}Pb-based DLL3-targeting RDT in its co-development program with Orano Med. The supporting preclinical data were presented at the Society of Nuclear Medicine and Molecular Imaging (SNMMI) 2024 Annual Meeting which took place in Toronto, Canada.

DLL3 is a priority target for radiopharmaceutical therapy based on its abundant expression in over 85% small cell lung cancer (SCLC) patients and other aggressive neuroendocrine tumors, while its expression in healthy tissues is low. SCLC is an aggressive form of lung cancer, with a poor five-year survival prognosis and a high unmet need for patients.

The data presented at SNMMI provide strong support for the clinical development of MP0712 in SCLC and other DLL3-expressing neuroendocrine tumors. *In vivo* data demonstrated strong and homogeneous tumor uptake, as well as substantial and durable inhibition of tumor growth at clinically relevant doses. Furthermore, the *in vivo* data suggested a favorable preclinical safety profile and support MP0712's potential for clinical use. Achieving favorable tumor to kidney ratios and biodistribution are key design objectives for this program. In both areas MP0712 performed well in mouse xenograft tumor models; tumor to kidney ratios over two were observed, and close to 60% of the injected dose per gram of tissue was detectable in the tumor.

The replicable learnings from the development and optimization of MP0712, as well as additional RDT platform improvements, are being taken forward to the broader RDT portfolio. Molecular Partners will present additional data in an oral presentation at the 2024 Congress of the European Association of Nuclear Medicine (EANM) in October 2024, and plans to initiate a first-in-human clinical trial of MP0712 in 2025.

In addition to the above updates, Molecular Partners continued to progress its RDT portfolio of projects in partnership with Novartis and is evaluating additional targets for RDT programs.

MP0533

MP0533, a novel tetra-specific T cell-engaging DARPin, is currently being evaluated in a Phase 1/2a clinical trial for patients with relapsed/refractory acute myeloid leukemia (r/r AML) and myelodysplastic syndrome/AML (MDS/AML) (ClinicalTrials.gov: NCT05673057). The mechanism of action of MP0533 is designed to preferentially kill AML cells (blasts, leukemic progenitor and stem cells) that express any combination of the three cell surface antigens CD33, CD123, and CD70, while sparing healthy cells, which tend to express only one or none of these targets. The immune activation against the malignant cells is achieved through CD3-mediated T cell-engagement.

In April 2024, comprehensive preclinical data supporting MP0533's proposed unique mechanism of action for the treatment of AML was published in *Cancer Immunology Research (https://doi.org/10.1158/2326-6066.CIR-23-0692)*, a journal of the American Association for Cancer Research.

In the ongoing Phase 1/2a clinical trial, as of 29 July 2024, MP0533 has demonstrated an acceptable safety profile with the majority of adverse events reported being infusion-related reactions and cytokine release syndrome. Four clinical responses have been observed among the 28 patients across dosing regimens (DR) 1–6. These included a complete response in DR 4 and a morphologic leukemia-free state in three patients, one each in DRs 3, 5 and 6. Furthermore, an encouraging trend in bone marrow blast cell reductions was observed as of the data cut-off date; 7 of 26 evaluable patients and 5 of 11 patients with low disease burden at baseline (blasts <20%) displayed a blast reduction over 50%.

At present, data are being collected for DR7 and dose escalation continues with DR 8 open. Based on the observed safety profile and encouraging initial antitumor activity data, and following discussion with treating physicians and key opinion leaders, Molecular Partners is amending the protocol to further increase dosing and improve the exposure profile of MP0533. The Company's aim is to achieve higher response rates, as well as improved depth and duration of responses in r/r AML patients. Molecular Partners plans to present a clinical update on the program in H2 2024, and on the amended dosing scheme for MP0533 in 2025.

Switch-DARPin Platform and first candidate MP0621

The Switch-DARPin platform represents a novel innovative DARPin-based approach by Molecular Partners that provides a logic-gated "on/off" function (the "Switch") to multispecific DARPin candidates, allowing target activation only in the presence of a defined set of antigens. The goal is conditional activation of a targeted immune response. The first Switch-DARPin program, MP0621 (cKit x CD16a x CD47), was introduced in January 2024 and is designed to induce killing of hematopoietic stem cells as a next-generation conditioning regimen. Molecular Partners' intends to extend access to potentially curative HSCT for more patients with AML as well as those with other hematologic malignancies or genetic diseases requiring HSCT.

In June 2024, the Company presented preclinical proof-of-concept data from MP0621 at the European Hematology Association (EHA) 2024 Hybrid Congress which took place in Madrid, Spain. The safety, efficacy and pharmacokinetic data supported MP0621's ability to selectively kill cKit positive cells and conditionally block the immunosuppressive protein CD47, with limited systemic side effects.

Crucially, these preclinical data also validated the Switch-DARPin concept, demonstrating that a logic-gated immune activation with a reversible switch can be achieved with a DARPin design. This provides another novel DARPin approach for conditional activation of anticancer immunotherapies and its utilization to locally engage immune-modulating targets not amenable to other treatment modalities. Further preclinical studies are ongoing with updates for the MP0621 program planned for H2 2024.

MP0317

MP0317 is a CD40 agonist designed to activate immune cells specifically within the tumor microenvironment (TME) by anchoring to fibroblast activation protein (FAP) which is expressed in high amounts around tumors. This tumor-localized approach has the potential to deliver greater efficacy with fewer side effects compared to systemic CD40-targeting therapies.

In June 2024, the Company presented positive data from its completed Phase 1 dose-escalation clinical trial of MP0317 at the American Society of Clinical Oncology (ASCO) Annual Meeting 2024 which took place in Chicago, IL, USA.

The final analysis included 46 patients with advanced solid tumors and confirmed earlier reported interim results. MP0317 displayed a favorable and manageable safety profile across all nine planned dosing cohorts (0.03–10 mg/kg) administered intravenously weekly or every 3 weeks with only one patient experiencing a dose-limiting toxicity (transient asymptomatic grade 3 elevation of liver enzymes). The most frequently observed adverse reactions were fatigue and lower grade infusion-related reactions (grade 1–2). MP0317 treatment resulted in target occupancy in tumor biopsies with evidence of TME remodeling. In terms of clinical response, one patient achieved an unconfirmed partial response and stable disease was observed in 14 additional patients.

The positive data support further clinical evaluation of MP0317 in combination with complementary anticancer therapies and demonstrated the ability of the DARPin design to deliver on a targeted, tumor-localized CD40 activation mechanism. Molecular Partners is in discussion with leading academic centers regarding potential investigator-initiated combination trials.

Corporate and Management Highlights

On August 26 2024, Philippe Legenne, M.D., MBA, MHS, acting CMO and SVP Medical Strategy and Development, was appointed Chief Medical Officer at MP. "I am grateful that Phillippe is stepping fully into the role of CMO. Under his leadership, our MP0533 program has enrolled all dose cohorts at maximum speed, strongly supported by our investigators. This was only possible by the stellar performance by Philippe's team. With his broad oncology background, ability to build a strong team and gift to engage trustfully with KOLs, he is in an ideal position to progress our first Radio-DARPin therapies towards clinical development in the months to come," said Patrick Amstutz, CEO of Molecular Partners.

Dr. Legenne joined Molecular Partners in early 2020. Over this time, he has led the clinical development strategy and execution across the Molecular Partners portfolio, including the successful initiation and seamless execution of MP0533, MP0317 and Ensovibep. Prior to joining Molecular Partners,

Philippe held positions of increasing responsibility at JNJ, GSK, and Novartis, both in the United States and Europe. In his most recent role prior to Molecular Partners, Philippe led the EU medical organization for the oncology portfolio at Amgen. He received his medical degree from the Université de Lille (France), an MBA from ESSEC Business School (Paris) and a Master's degree in health economics from Université Paris Dauphine-PSL.

As previously communicated, a putative class action complaint filed in July 2022 in the U.S. District Court for the Southern District of New York was dismissed without prejudice in the Company's favor in February 2024 and was subsequently ordered closed.

At the Company's Annual General Meeting on April 17, 2024, all motions proposed by the Board of Directors at the Annual General Meeting were approved by the shareholders of the Company.

H1 2024 Operational and Financial Highlights

- Strong financial position with CHF 159.1 million in cash (including short term deposits) as of June 30, 2024
- Net cash used in operating activities of CHF 32.8 million in H1 2024
- Operating loss of CHF 31.8 million and net loss of CHF 26.4 million in H1 2024
- Company expected to be funded into 2027, excluding any potential payments from R&D partnerships

The H1 2024 Financial Statements are available on the company's website.

Key figures as of June 30, 2024 (unaudited) (CHF million, except per share, FTE data)	**H1 2024**	**H1 2023**	**Change**
Total revenues and other income	**4.3**	**3.5**	**0.8**
R&D expenses	(27.2)	(24.3)	(2.9)
SG&A expenses	(8.9)	(10.2)	1.2
Operating result	**(31.8)**	**(31.0)**	**(0.8)**
Net result	**(26.4)**	**(30.8)**	**4.4**
Basic and diluted net result per share (in CHF)	(0.80)	(0.94)	0.14
Net cash from (used in) operating activities	**(32.8)**	**(29.8)**	**(2.9)**
Cash balance (incl. time deposits) as of June 30	**159.1**	**218.2**	**(59.1)**
Total shareholders' equity as of June 30	**155.6**	**206.0**	**(50.4)**
Number of total FTE as of June 30	**161.9**	**168.5**	**(6.6)**

Business Outlook and Priorities
Molecular Partners continues its strategic focus on areas of maximum differentiation by virtue of the DARPins' unique properties. The Company expects its cash position provides the flexibility to execute on its development priorities efficiently and effectively within this focus, with funding to support portfolio development forecasted into 2027. In addition to its two existing clinical-stage programs, the Radio-DARPin Therapy and Switch-DARPin platforms have been further substantiated by maturing data as sources of growth for the Company's portfolio. As a whole, Molecular Partners remains well positioned to significantly grow through developmental milestones, new candidates and potential partnerships.

Financial Outlook 2024
For 2024, at constant exchange rates, the Company expects total expenses of CHF 65 - 75 million (previously estimated at CHF 70 - 80 million), of which approximately CHF 8.0 million will be non-cash effective costs for share-based payments, IFRS pension accounting and depreciation. This guidance does not include any potential receipts from R&D partnerships.

With CHF 159.1 million in cash and short-term time deposits and no debt as of June 30, 2024, the Company expects to be funded into 2027, excluding any potential receipts from R&D partners.

The Company's balance sheet continued to be debt-free in 2024. As of June 30, 2024, the Company employed 161.9 FTE (full time equivalents), down 4% year-on-year. About 84% of the employees are employed in R&D-related functions.

Documentation
The results presentation, this press release, and the H1 2024 report will be made available on www.molecularpartners.com after 10:00pm (CET) on August 26, 2024.

H1 2024 Conference Call & Audio Webcast
Molecular Partners will hold a conference call and audio webcast on August 27, 2024, 2:00pm CET (8:00am EST). To register for the H1 2024 conference call, please dial the following numbers approximately 10 minutes before the start of the presentation:

Switzerland / Europe:	+41 44 575 0267
USA:	+1 844 763 8274
UK:	+44 20 3795 9972

Financial calendar

October 31, 2024	Interim Management Statement Q3 2024
March 12, 2025	Full-year results 2024

The latest timing of the above events can be viewed on the investor section of the website.

About DARPin Therapeutics
DARPin (Designed Ankyrin Repeat Protein) therapeutics are a new class of custom-built protein drugs based on natural binding proteins that open new dimensions of multi-functionality and multi-target specificity in drug design. The flexible architecture, intrinsic potential for high affinity and specificity, small size and high stability of DARPins offer benefits to drug design over other currently available protein-based therapeutics. DARPin candidates can be radically simple, with a single DARPin unit acting as the delivery vector to a specific target; or multispecific, with the possibility of engaging more than five targets, and combining multiple and conditional functionalities in a unique DARPin drug candidate. The DARPin platform is designed to be a rapid and cost-effective drug discovery engine, producing drug candidates with optimized properties and high production yields. DARPin therapeutics have been clinically validated across several therapeutic areas and developed through to the registrational stage.

About Molecular Partners AG
Molecular Partners AG is a clinical-stage biotech company pioneering the design and development of DARPin therapeutics for medical challenges other drug modalities cannot readily address. The Company has programs in various stages of pre-clinical and clinical development, with oncology as its main focus. Molecular Partners leverages the advantages of DARPins to provide unique solutions to patients through its proprietary programs as well as through partnerships with leading pharmaceutical companies. Molecular Partners was founded in 2004 and has offices in both Zurich, Switzerland and Concord, MA, USA. For more information, visit www.molecularpartners.com and find us on LinkedIn and Twitter/X @MolecularPrtnrs

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Cautionary Note Regarding Forward-Looking Statements
Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation: implied and express statements regarding the clinical development of Molecular Partners' current or future product candidates; expectations regarding timing for reporting data from ongoing clinical trials or the initiation of future clinical trials; the potential therapeutic and clinical benefits of Molecular Partners' product candidates and its RDT and Switch-DARPin platforms; the selection and development of future programs; Molecular Partners' collaboration with Orano Med including the benefits and results that may be achieved through the collaboration; and Molecular Partners' expected business and financial outlook, including anticipated expenses and cash utilization for 2024 and its expectation of its current cash runway. These statements may be identified by words such as "aim", "expect", "guidance", "intend", "outlook", "plan", "potential", "will" and similar expressions, and are based on Molecular Partners' current beliefs and expectations. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Some of the key factors that could cause actual results to differ from Molecular Partners' expectations include its plans to develop and potentially commercialize its product candidates; Molecular Partners' reliance on third party partners and collaborators over which it may not always have full control; Molecular Partners' ongoing and planned clinical trials and preclinical studies for its product candidates, including the timing of such trials and studies; the risk that the results of preclinical studies and clinical trials may not be predictive of future results in connection with future clinical trials; the timing of and Molecular Partners' ability to obtain and maintain regulatory approvals for its product candidates; the extent of clinical trials potentially required for Molecular Partners' product candidates; the clinical utility and ability to achieve market acceptance of Molecular Partners' product candidates; the potential that Molecular Partners' product candidates may exhibit serious adverse, undesirable or unacceptable side effects; the impact of any health pandemic, macroeconomic factors and other global events on Molecular Partners' preclinical studies, clinical trials or operations, or the operations of third parties on which it relies; Molecular Partners' plans and development of any new indications for its product candidates; Molecular Partners' commercialization, marketing and manufacturing capabilities and strategy; Molecular Partners' intellectual property position; Molecular Partners' ability to identify and in-license additional product candidates; unanticipated factors in addition to the foregoing that may impact Molecular Partners' financial and business projections and guidance; and other risks and uncertainties that are described in the Risk Factors section of Molecular Partners' Annual Report on Form 20-F for the fiscal year ended December 31, 2023, filed with Securities and Exchange Commission (SEC) on March 14, 2024 and other filings Molecular Partners makes with the SEC. These documents are available on the Investors page of Molecular Partners' website at www.molecularpartners.com. In addition, this press release contains information relating to interim data as of the relevant data cutoff date, results of which may differ from topline results that may be obtained in the future. Any forward-looking statements speak only as of the date of this press release and are based on information available to Molecular Partners as of the date of this release, and Molecular Partners assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.