Insmed Unveils New Research Platforms and Capabilities at Investor and Analyst Event, "The Future of Rare at Insmed: Functional Genes, AI-Enhanced Proteins, Glowing Algae, and More"

—Early-Stage Research Pillar Anticipated to Generate at Least Six Investigational New Drug (IND) Applications by End of 2025—

—Company Reveals Select Initial Disease Targets for Next-Generation Gene Therapies and Deimmunized Therapeutic Proteins, Including Duchenne Muscular Dystrophy (DMD) and Stargardt Disease—

—Gene Therapy Clinical Trial in DMD to be Initiated in 2023, with Data Expected First Half of 2024—

—Company Announces $500,000 Equity Investment from CureDuchenne Ventures to Support the Development of a Targeted Gene Therapy for DMD—

BRIDGEWATER, N.J., May 8, 2023 /PRNewswire/ -- Insmed Incorporated (Nasdaq: INSM), a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases, today announced progress across its early-stage research programs, which will be discussed in greater detail this morning at the Company's investor and analyst event, *The Future of Rare at Insmed: Functional Genes, AI-Enhanced Proteins, Glowing Algae, and More*. The event will feature presentations from Insmed's management team and scientific leaders as well as from John W. Day, M.D., Ph.D., Professor of Neurology, Pediatrics, and Pathology at Stanford University, and Michael G. Kelly, Ph.D., Chief Scientific Officer of CureDuchenne, a leading global nonprofit focused on finding and funding a cure for Duchenne muscular dystrophy (DMD).

"Our singular focus at Insmed has always been on patients – developing and delivering therapies that will make a transformational impact on their lives, regardless of modality or therapeutic area," said Will Lewis, Chair and Chief Executive Officer of Insmed. "Across our first three pillars, this has been the standard against which we have measured success, and we have proven our ability to deliver on our promise to patients at every stage of drug development and commercialization. Today, I look forward to unveiling the unique platforms and capabilities that will fuel our next phase of growth and, together with our first three pillars, put us on the path to become one of the next great, sustainable biotechnology companies. Driven by our highly skilled, industry-leading research teams, we believe the technologies we are progressing can address the challenges facing today's gene therapies and therapeutic proteins to deliver the next generation of first-in-class, first-in-disease, and potentially best-in-class medicines."

Select Highlights from 'The Future of Rare at Insmed':

Gene Therapy with Targeted Delivery

Insmed has developed a targeted adeno-associated virus (AAV) delivery system to potentially address some of the key challenges associated with current gene therapies, including high dose requirements, inherent systemic toxicities, low efficacy, and off-target transduction. This targeted mode of delivery has the potential to reduce the needed dose 10- to 50-fold, which may in turn offer an enhanced safety profile without limiting efficacy. Key updates from this platform include:

- Insmed's first gene therapy candidate using a targeted intrathecal delivery approach will be in DMD, a devastating genetic disorder characterized by progressive muscle degeneration and weakness.
- The Company announced a $500,000 equity investment from CureDuchenne Ventures, the investment arm of CureDuchenne, to support the development of Insmed's gene therapy program for DMD.
- Insmed plans to initiate a gene therapy clinical trial in DMD later this year, with muscle biopsy data expected in the first half of 2024.
- Additional gene therapy targets have been identified and preclinical work is underway.
- Insmed has created an end-to-end gene therapy manufacturing process designed to be scalable, reproducible, and able to meet commercial demand and quality standards. This includes development of a 1,000-liter suspension-based bioreactor manufacturing process and in-house GMP quality control laboratory to disposition AAV drug product.

"While exciting advances have led to clinical trials of gene replacement approaches for DMD, the current landscape is complicated by requiring high doses of viral vectors that raise safety and tolerability concerns, resulting in significant debate and lack of clarity on how best to manage patients with this devastating disease," noted Dr. Day. "The possibility of a more targeted, lower-dose therapy that could reduce systemic toxicity and provide a safer option for patients is very promising. While the gene therapy approaches discussed today are still in development, I am confident the entire neurogenetic community will be watching closely to see what possibilities this research opens for individuals living with DMD or other genetic disorders."

RNA End-Joining (REJ) Technology

Insmed's REJ technology has the potential to enable large-size gene delivery, overcoming the capacity challenges associated with traditional AAV vectors. This technology may make it possible to employ gene therapy for diseases caused by large genes that have historically not been viable targets for AAV gene therapy. Key updates from this platform include:

- Insmed plans to target Stargardt disease, a hereditary retinal disease that causes vision loss typically beginning in childhood, with its first REJ gene therapy candidate. Patients with Stargardt disease currently have no approved therapies to treat their condition.
- The Company expects to submit an IND for the treatment of Stargardt disease by the end of 2024.
- Insmed is also exploring the potential of REJ to deliver larger dystrophin protein in DMD.
- Evaluation of additional REJ targets is currently underway.

Protein Deimmunization

Insmed's proprietary protein deimmunization platform, Deimmunized by Design® (DbD), offers a potential solution to the immunogenicity challenges associated with both gene therapies and protein therapeutics by using artificial intelligence to reengineer proteins to silence their immunogenic properties while maintaining their therapeutic activity. Using this platform, Insmed is actively deimmunizing several therapeutic proteins and viral vectors, including AAV capsids, which could unlock the potential for redosable gene therapy. Key updates from this platform include:

- Insmed is exploring the potential of redosable gene therapy using a deimmunized AAV capsid in the treatment of argininosuccinic aciduria (ASA), a rare, devastating urea cycle disorder that typically presents in newborns, and expects to have preclinical data in 2024.
- Insmed is also exploring the potential of a deimmunized variant of uricase, a therapeutic protein, in the treatment of chronic refractory gout, and expects to have preclinical data in 2024.
- Additional therapeutic proteins are currently under development.

Proprietary Manufacturing

Insmed is advancing a proprietary manufacturing technique that leverages the unique properties of algae to potentially reduce the time, cost, and complexity of producing therapeutic proteins and viral vectors for gene therapy. This next-generation approach may offer potential benefits including rapid scalability, no plasmid transfection, low production costs, and ease of culturing and maintenance. Insmed expects to advance to full AAV capsid production using this manufacturing platform in 2024.

Live Webcast

'The Future of Rare at Insmed' will take place today from 8:00 a.m. to 12:00 p.m. ET in person and via webcast. The event and accompanying slides will be streamed live on the Investor Relations section of the Company's website at www.insmed.com. A replay of the event will be accessible approximately 30 minutes after its completion. A copy of the presentation materials and webcast will be archived for 90 days under the Investor Relations section of the Company's website at www.insmed.com.

About Insmed

Insmed Incorporated is a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. Insmed's first commercial product is a first-in-disease therapy approved in the United States, Europe, and Japan to treat a chronic, debilitating lung disease. The Company is also progressing a robust pipeline of investigational therapies targeting areas of serious unmet need, including neutrophil-mediated inflammatory diseases and rare pulmonary disorders. Insmed is headquartered in Bridgewater, New Jersey, with a footprint across Europe and in Japan. For more information, visit www.insmed.com.

Forward-looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) may identify forward-looking statements.

The forward-looking statements in this press release are based upon the Company's current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause the Company's actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timings discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside the U.S., Europe or Japan, or for the Company's product candidates in the U.S., Europe, Japan or other markets, including separate regulatory approval for the Lamira® Nebulizer System in each market and for each usage; failure to successfully commercialize ARIKAYCE, the Company's only approved product, in the U.S., Europe or Japan (amikacin liposome inhalation suspension, Liposomal 590 mg Nebuliser Dispersion, and amikacin sulfate inhalation drug product, respectively), or to maintain U.S., European or Japanese approval for ARIKAYCE; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; impact of the COVID-19 pandemic and efforts to reduce its spread on the Company's business, employees, including key personnel, patients, partners and suppliers; risk that brensocatib or TPIP does not prove to be effective or safe for patients in ongoing and future clinical studies, including, for brensocatib, the ASPEN study; uncertainties in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community; the Company's inability to obtain full approval of ARIKAYCE from the U.S. Food and Drug Administration, including the risk that the Company will not successfully or in a timely manner complete the study to validate a patient reported outcome tool and the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE; inability of the Company, PARI or the Company's other third-party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira® Nebulizer System; the Company's inability to obtain adequate reimbursement from government or third-party payors for ARIKAYCE or acceptable prices for ARIKAYCE; development of unexpected safety or efficacy concerns related to ARIKAYCE, brensocatib, TPIP or the Company's other product candidates; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE, brensocatib, TPIP or the Company's other product candidates or in data the Company has used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; the risks and uncertainties associated with, and the perceived benefits of, the Company's secured senior loan with certain funds managed by Pharmakon Advisors, LP and the Company's royalty financing with OrbiMed Royalty & Credit Opportunities IV, LP, including our ability to maintain compliance with the covenants in the agreements for the senior secured loan and royalty financing and the perceived impact of the restrictions on the Company's operations under these agreements; the Company's inability to create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE or any of the Company's product candidates that are approved in the future; failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; risk that the Company's competitors may obtain orphan drug exclusivity for a product that is essentially the same as a product the Company is developing for a particular indication; failure to successfully predict the time and cost of development, regulatory approval and commercialization for novel gene therapy products; failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib, TPIP and the Company's other product candidates due to the Company's limited experience in conducting preclinical development activities and clinical trials necessary for regulatory approval and its potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval, among other things; risks that the Company's clinical studies will be delayed or that serious side effects will be identified during drug development; failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE or the Company's product candidates for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with the Company's agreements or laws and regulations that impact the Company's business or agreements with the Company; the Company's inability to attract and retain

key personnel or to effectively manage the Company's growth; the Company's inability to successfully integrate its recent acquisitions and appropriately manage the amount of management's time and attention devoted to integration activities; risks that the Company's acquired technologies, products and product candidates are not commercially successful; the Company's inability to adapt to its highly competitive and changing environment; risk that the Company is unable to maintain its significant customers; risk that government healthcare reform materially increases the Company's costs and damages its financial condition; deterioration in general economic conditions in the U.S., Europe, Japan and globally, including the effect of prolonged periods of inflation, affecting the Company, its suppliers, third-party service providers and potential partners; the Company's inability to adequately protect its intellectual property rights or prevent disclosure of its trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters; restrictions or other obligations imposed on the Company by agreements related to ARIKAYCE or the Company's product candidates, including its license agreements with PARI and AstraZeneca AB, and failure of the Company to comply with its obligations under such agreements; the cost and potential reputational damage resulting from litigation to which the Company is or may become a party, including product liability claims; risk that the Company's operations are subject to a material disruption in the event of a cybersecurity attack or issue; business disruptions or expenses related to the upgrade to the Company's enterprise resource planning system; the Company's limited experience operating internationally; changes in laws and regulations applicable to the Company's business, including any pricing reform, and failure to comply with such laws and regulations; the Company's history of operating losses, and the possibility that the Company may never achieve or maintain profitability; goodwill impairment charges affecting the Company's results of operations and financial condition; inability to repay the Company's existing indebtedness and uncertainties with respect to the Company's ability to access future capital; and delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities and unexpected expenses associated with those plans.

The Company may not actually achieve the results, plans, intentions or expectations indicated by the Company's forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. For additional information about the risks and uncertainties that may affect the Company's business, please see the factors discussed in Item 1A, "Risk Factors," in the Company's Annual Report on Form 10-K for the year ended December 31, 2022 and any subsequent Company filings with the Securities and Exchange Commission (SEC).

The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date of this press release. The Company disclaims any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

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