NEWS RELEASE

# Inovio Presents Cancer Killing Data of Its Transformative DNA-Encoded Bi-specific T Cell Engagers (dBiTEs) at AACR

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Data demonstrates tumor-clearing ability of Inovio's dBiTE technology in preclinical cancer model

PLYMOUTH MEETING, Pa., April 2, 2019 /PRNewswire/ -- Inovio Pharmaceuticals, Inc. (NASDAQ: INO) announced today the company's novel DNA-Encoded Bi-specific T Cell Engagers (dBiTEs™) generated potent anti-tumor activities in a preclinical study. Results were presented as a poster at the American Association for Cancer Research (AACR) Annual Meeting in Atlanta. For this study, Inovio, with its collaborators at The Wistar Institute, developed a novel dBiTE targeting the HER2 molecule which was tested in therapeutic models for the treatment of ovarian and breast cancers. Importantly, just a single dose of Inovio's HER2 dBiTE resulted in high levels of corresponding BiTE in mice for four months, far exceeding what is typically displayed with conventional BiTE's short half-life of only a few hours. The HER2 dBiTE effectively generated T cell cytotoxicity against HER2-expressing tumor cells resulting in a near-complete tumor clearance. Also presented was Inovio's CD19 dBiTE which can kill B cell cancers by targeting B cell specific marker CD19.

Dr. J. Joseph Kim, Inovio's President and CEO, said, "In layman's terms, dBiTEs are like a double-sided tape that binds to a tumor and to a cancer-killing T cell. By allowing the products be expressed directly and efficiently in the patient, our dBiTEs could finally fulfill the therapeutic promise of BiTEs. Based on these promising preclinical results, we are rapidly preparing for the clinical development of our dBiTE candidates, as well as constructing more cancer tumor targeting dBiTE candidates using our transformative dBiTE platform."

Dr. Kim added, "Leveraging Inovio's in vivo synthetic nucleic expression platform, we have shown that just one dose of Inovio's dBiTE could generate corresponding BiTEs at high levels in mice for several months, demonstrating a dramatic advantage over conventional BiTEs. Our CD19 dBiTE has the potential to treat multiple B cell cancers and to compete favorably with CD19 CAR-T products with potentially improved tolerability and safety profiles. Similarly, the HER2 dBiTE could be used to treat multiple solid tumors which express HER2 such as breast, ovarian, and gastric cancers."

BiTEs are a class of artificial bi-specific monoclonal antibodies that has the potential to transform the immunotherapy landscape for cancer. They direct a host's immune system, more specifically the T cells' cytotoxic activity, against cancer cells. BiTEs have two

binding domains. One domain binds to the targeted tumor (like HER2 or CD19 expressing cells) while the other engages the immune system by binding directly to CD3 molecules on T cells. This double-binding activity drives T cell activation directly at the tumor resulting in a killing function and tumor destruction.

The biggest drawback of conventional protein-based BiTEs is the delivery and expression. The BiTEs have a half-life of only about two hours, which requires patients to undergo continuous intravenous infusion for several weeks to maintain therapeutic levels, making treatment adherence more difficult and resulting in high levels of infusion-associated adverse events. In addition, just like other traditional monoclonal antibodies, conventional BiTEs are also manufactured in bioreactors, typically requiring costly large-scale manufacturing facility development and laborious production as well as having to deal with improper product folding and stability. They must also be kept and distributed frozen at all times. These difficulties collectively have limited the development and commercialization of conventional BiTEs as only one licensed product is currently on the market (BLINCYTO® (blinatumomab)).

Inovio's dBiTE is a new transformative application of Inovio's dMAb™ platform. The dBiTEs share many advantages of Inovio's dMAbs as they both are composed of engineered DNA sequences which encode two antibody fragments. When administered by Inovio's CELLECTRA® delivery device, the patient's own cells become the factory to manufacture functional BiTES encoded by the delivered dBiTE sequences.

Inovio's dBiTEs provide major potential advantages over a conventional protein-based BiTE therapy because of dBiTEs' better product expression and availability as well as simplicity in administration and manufacturing.  Inovio has demonstrated that a single dose of dBiTE construct delivered with CELLECTRA® expressed the product at high levels in mice for four months. Inovio's dBiTEs are developed with simplified design using novel plasmid vectors and unique formulations allowing for rapidity of development, long-term product stability at refrigeration, ease of validated and scalable manufacturing and deployability.

Earlier this year, Inovio initiated the first clinical trial for a dMAb. Funded fully by the Bill & Melinda Gates Foundation, this trial's focus is on evaluating the dMAb's (INO-A002) ability to prevent or treat Zika virus infection. The clinical results will help to broadly advance Inovio's dMAb and dBiTE programs in infectious diseases and cancer.

## About Inovio's dBiTE program

Inovio's dBiTEs are able to target the cytotoxic T cells to tumors by engaging proteins expressed in the tumor surface. The current preclinical models have shown proof that DNA technologies are in an advantageous position to launch a more ambitious BiTE program. The tumor-binding domain can be modified to engage multiple targets, of which preclinical data targeting HER2 and CD19 will be presented. Of these, the CD19dBiTE can be used to target B cell cancers and the HER2dBiTE can be used to treat advanced breast, ovarian, gastric, esophageal and endometrioid cancers.

## About Inovio Pharmaceuticals, Inc.

Inovio is a late-stage biotechnology company focused on the discovery, development, and commercialization of DNA-based immunotherapies and vaccines that transform the treatment and prevention of cancer and infectious disease. Inovio's proprietary technology platform applies antigen sequencing and DNA delivery to activate potent immune responses to targeted diseases. The technology functions exclusively in vivo, and has been demonstrated to consistently activate robust and fully functional T cell and antibody responses against targeted cancers and pathogens. Inovio's most advanced clinical program, VGX-3100, is in Phase 3 for the treatment of HPV-related cervical pre-cancer. Also in development are Phase 2 immuno-oncology programs targeting HPV-related cancers, bladder cancer, and glioblastoma, as well as platform development programs in hepatitis B, Zika, Ebola, MERS, and HIV. Partners and collaborators include AstraZeneca, Regeneron, Roche/Genentech, ApolloBio Corporation, The Wistar Institute, The Bill & Melinda Gates Foundation, the University of Pennsylvania, Parker Institute for Cancer Immunotherapy, CEPI, DARPA, GeneOne Life Science, Plumbline Life Sciences, NIH, HIV Vaccines Trial Network, National Cancer Institute, Walter Reed Army Institute of Research, Drexel University, and Laval University. For more information, visit **www.inovio.com**.

This press release contains certain forward-looking statements relating to our business, including our plans to develop electroporation-based drug and gene delivery technologies and DNA vaccines, our expectations regarding our research and development programs, including the planned initiation and conduct of clinical trials and the availability and timing of data from those trials. Actual events or results may differ from the expectations set forth herein as a result of a number of factors, including uncertainties inherent in pre-clinical studies, clinical trials and product development programs, the availability of funding to support continuing research and studies in an effort to prove safety and efficacy of electroporation technology as a delivery mechanism or develop viable DNA vaccines, our ability to support our pipeline of SynCon® active immunotherapy and vaccine products, the ability of our collaborators to attain development and commercial milestones for products we license and product sales that will enable us to receive future payments and royalties, the adequacy of our capital resources, the availability or potential availability of alternative therapies or treatments for the conditions targeted by us or our collaborators, including alternatives that may be more efficacious or cost effective than any therapy or treatment that we and our collaborators hope to develop, issues involving product liability, issues involving patents and whether they or licenses to them will provide us with meaningful protection from others using the covered technologies, whether such proprietary rights are enforceable or defensible or infringe or allegedly infringe on rights of others or can withstand claims of invalidity and whether we can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of our technology by potential corporate or other partners or collaborators, capital market conditions, the impact of government healthcare proposals and other factors set forth in our Annual Report on Form 10-K for the year ended December 31, 2018 and other regulatory filings we make from time to time. There can be no assurance that any product candidate in our pipeline will be successfully developed, manufactured or commercialized, that final results of clinical trials will be supportive of regulatory approvals required to market licensed products, or that any of the forward-looking information provided herein will be proven accurate. Forward-looking statements speak only as of the date of this release, and we undertake no obligation to update or revise these statements, except as may be required by law.

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