Fusion Pharmaceuticals Announces Clinical Program And Manufacturing Updates

- ***Aligned with the FDA on submitted protocol for ^{225}Ac-PSMA (FPI-2265) Phase 2/3 registrational program for patients with metastatic castration-resistant prostate cancer (mCRPC)***
- ***Achieved target enrollment in ongoing TATCIST trial evaluating FPI-2265; Interim Phase 2 data expected to be presented in April 2024***
- ***FPI-1434 shows promising safety profile and early evidence of antitumor activity at 25 kBq/kg dose level***
- ***Fusion's state-of-the-art manufacturing facility now fully operational with first clinical dose produced***

HAMILTON, ON and BOSTON, Jan. 4, 2024 /PRNewswire/ -- Fusion Pharmaceuticals Inc. (Nasdaq: FUSN), a clinical-stage oncology company focused on developing next-generation radiopharmaceuticals as precision medicines, today announced significant progress with its FPI-2265 development program, an update on FPI-1434 Phase 1 Cohort 2 data and the production of the first clinical doses at the Company's proprietary manufacturing facility.

"We begin 2024 with strong momentum, given a potential registration-enabling path for FPI-2265, encouraging results in our FPI-1434 program, including first signs of antitumor activity, and a fully operational TAT manufacturing facility that has already begun to produce clinical doses for our actinium-based PSMA lead program," said Chief Executive Officer John Valliant, Ph.D.

"We achieved alignment with the U.S. Food and Drug Administration (FDA) on a protocol and development plan for FPI-2265, providing our team with a potential path to registration and positioning FPI-2265 to be the first actinium-based PSMA targeting radioligand therapy to market, if approved. Given the significant and growing market for PLUVICTO™, we believe that FPI-2265 will address an important unmet need for patients who progress on or after lutetium-based therapy."

FPI-2265 Phase 2/3 Development Plan in mCRPC

The Company announced today that it has aligned with the FDA on its submitted Phase 2/3 protocol for FPI-2265, a targeted alpha therapy (TAT) targeting prostate specific membrane antigen (PSMA) for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) with progressive disease. The updated development plan includes a Phase 2 dose optimization lead-in, expected to complete enrollment by the end of 2024, and a Phase 3 registrational trial expected to begin in 2025.

The Phase 2 portion of the protocol is designed to evaluate the safety and efficacy of FPI-2265 across three dosing regimens in approximately 60 patients with mCRPC with progressive disease after ^{177}Lu-based PSMA radioligand therapy, such as PLUVICTO™. Based on literature and TATCIST data reported to date, 100 kBq/kg administered every 8 weeks is known to be a safe and active dose regimen. In order to further optimize the benefit/risk ratio of FPI-2265, Fusion will explore alternate regimens with higher dosing frequency while keeping cumulative dose and total duration of treatment the same. Additional regimens to be evaluated will include a dose of 50 kBq/kg every 4 weeks and 75 kBq/kg every 6 weeks. The primary endpoints are safety and the proportion of patients with ≥ 50% decline in PSA level with key secondary endpoints of objective response rate (ORR) and radiographic progression free survival (rPFS). The Phase 2 trial is expected to initiate in the second quarter of 2024 with enrollment completed by year-end. The Company will seek to hold an End of Phase 2 meeting with the FDA to determine the recommended Phase 3 dosing regimen based on analysis of the Phase 2 data.

"We believe evaluating dosing regimens that deliver the same total dose over the same duration of treatment in the Phase 2 portion of the study allows us to optimize our Phase 3 clinical trial dose in alignment with FDA guidance and determine the best potential regimen of FPI-2265," said Chief Medical Officer, Dmitri Bobilev, M.D.

The Phase 3 portion of the trial is designed to be a registration-enabling global trial evaluating the efficacy and safety of FPI-2265 compared with standard of care in approximately 550 patients with mCRPC with progressive disease who have previously been treated with a ^{177}Lu-based PSMA radiotherapy. The primary endpoint will

evaluate rPFS. Key secondary endpoints include PFS, ORR, OS, PSA_{50} and duration of response. The Company plans to initiate the Phase 3 trial in 2025.

In February 2023, Fusion acquired an IND for the ongoing Phase 2 clinical trial (the TATCIST trial) evaluating FPI-2265 (^{225}Ac-PSMA I&T). The TATCIST trial was designed to evaluate patients with mCRPC with progressive disease, including patients who are naïve to PSMA-targeted radiopharmaceuticals and those who have been pre-treated with ^{177}Lu-based PSMA radiopharmaceutical therapy. Fusion intends to report data from approximately 25 to 30 patients in April 2024 and then prioritize enrollment in the new Phase 2/3 trial.

The Company is also pursuing the opportunity to potentially move the therapy candidate into earlier lines of treatment with combinations of FPI-2265 and olaparib. Fusion expects to initiate a combination trial in the first half of this year.

FPI-1434 Cohort 2 Data & Next Steps

Fusion announced today encouraging early findings from Cohort 2 in the ongoing FPI-1434 Phase 1 clinical trial. No dose limiting toxicities (DLTs) were observed to date in the 25 kBq/kg dose cohort. Two out of three patients completed the DLT period, and one pancreatic cancer patient discontinued treatment due to disease progression.

One heavily treated patient with Ewing sarcoma showed evidence of anti-tumor activity after a single 25 kBq/kg dose of FPI-1434. The second patient received four cycles of therapy and showed stable disease as best response. FPI-1434 was well tolerated, with no DLTs and transient Grade 1 or less thrombocytopenia at the 25 kBq/kg dose level.

The Company plans to complete and further evaluate results from Cohort 2 and hold a Safety Review Committee (SRC) meeting to evaluate the emerging data. Fusion plans to share more details on the data and the FPI-1434 development program in mid-2024.

Dr. Valliant continued, "We continue to believe alpha emitters represent the evolution of the toxin used in antibody-drug conjugates (ADCs) and hold the potential to improve the potency of naked antibodies. There is significant untapped potential to use the precision targeting of antibodies to deliver the potent payload of actinium directly to tumor cells. While early, we are encouraged by the results showing good safety and evidence of antitumor activity at low doses of FPI-1434."

In June 2023, Fusion reported results from three patients at 15 kBq/kg in Cohort 1 of the cold/hot dosing regimen. In Cohort 1, cold/hot dosing was observed to be generally well tolerated with no treatment-related serious adverse events (SAEs) or dose DLTs. Pre-administration of cold antibody demonstrated improved tumor uptake while also reducing hematological toxicity observed in the hot only dosing arm. Two heavily pre-treated patients from the cold/hot dosing arm received three and five cycles of treatment, with both achieving durable stable disease as their best response.

Manufacturing Facility Update

Fusion reported today that it has completed validation of its state-of-the-art good manufacturing practice (GMP) manufacturing facility and produced the first clinical dose of a TAT.

Dr. Valliant continued, "The initiation of production at our own facility, and the diversification afforded by our external partnerships, positions us for execution on our multiple clinical programs. We built Fusion on a foundation of end-to-end manufacturing expertise, including experience with global radiopharmaceutical logistics and distribution. We also now have one of the first in-house TAT manufacturing facilities with access to a generator technology that allows for convenient onsite production of actinium-225, providing us with additional capacity and flexibility in our manufacturing programs."

Fusion's facility, which has clinical and commercial scale manufacturing capabilities, is designed to support the Company's growing pipeline of TATs and expected to be capable of producing up to 100,000 doses per year. Doses produced out of Fusion's manufacturing facility are expected to support FPI-2265 manufacturing and are expected to be expanded to include Fusion's other proprietary and partnered programs.

Financials

On a pro forma basis as of September 30, 2023, Fusion's cash, cash equivalents and investments were approximately $287 million, after taking into account subsequent proceeds of approximately $65 million from sales under the Company's at-the-market equity offering program and an expected $15 million draw down under the Company's existing debt facility. Fusion expects its cash, cash equivalents and investments will now be sufficient to fund operating expenses and capital expenditure requirements into the fourth quarter of 2025.

About Fusion

Fusion Pharmaceuticals is a clinical-stage oncology company focused on developing next-generation radiopharmaceuticals as precision medicines. Fusion connects alpha particle emitting isotopes to various targeting molecules in order to selectively deliver the alpha emitting payloads to tumors. Fusion's clinical portfolio includes: FPI-2265 targeting prostate specific membrane antigen (PSMA) for metastatic castration resistant prostate cancer currently in a Phase 2 trial; FPI-1434 targeting insulin-like growth factor 1 receptor currently in a Phase 1 clinical trial; and FPI-2059, a small molecule targeting neurotensin receptor 1 (NTSR1), currently in a Phase 1 trial. In addition to a robust proprietary pipeline, Fusion has a collaboration with AstraZeneca to jointly develop novel targeted alpha therapies (TATs) and combination programs between Fusion's TATs and AstraZeneca's DNA Damage Response Inhibitors (DDRis) and immuno-oncology agents. The Company received IND clearance for FPI-2068, the first novel TAT under the collaboration, which targets EGFR-cMET. Fusion has also entered into a collaboration with Merck to evaluate FPI-1434 in combination with Merck's KEYTRUDA® (pembrolizumab) in patients with solid tumors expressing IGF-1R. Fusion leases a current Good Manufacturing Practice (GMP) compliant radiopharmaceutical manufacturing facility designed to support manufacturing of the Company's growing pipeline of TATs on the McMaster University campus in Hamilton, Ontario. To support Fusion's growing pipeline of TATs, the Company has signed strategic actinium supply agreements with Niowave, Inc. and BWXT Medical.

Forward-Looking Statements

This press release contains "forward-looking statements" for purposes of the safe harbor provisions of The Private Securities Litigation Reform Act of 1995, including but not limited to the statements regarding the future business and financial performance of Fusion Pharmaceuticals Inc. (the "Company"). For this purpose, any statements contained herein that are not statements of historical fact may be deemed forward-looking statements. Without limiting the foregoing, the words "expect," "plans," "anticipates," "intends," "will," and similar expressions are also intended to identify forward-looking statements, as are expressed or implied statements with respect to the Company's financial condition, liquidity, and potential drug candidates, including any expressed or implied statements regarding the successful development of FPI-2265 or FPI-1434. Actual results may differ materially from those indicated by such forward-looking statements as a result of risks and uncertainties, including but not limited to the following: there can be no guarantees that the Company will advance any clinical product candidate or other component of its potential pipeline in or to the clinic, to the regulatory process or to commercialization; management's expectations could be affected by unexpected patient recruitment delays or regulatory actions or delays; uncertainties relating to, or unsuccessful results of, clinical trials, including additional data relating to the ongoing clinical trials evaluating its product candidates; the Company's ability to obtain additional funding required to conduct its research, development and commercialization activities; changes in the Company's business plan or objectives; competition in general; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for its product candidates and its discoveries; and the Company partners' ability to advance any technology relating to actinium-225 to development. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. These and other risks which may impact management's expectations are described in greater detail under the heading "Risk Factors" in the Company's quarterly report on Form 10-Q for the period ended September 30, 2023, as filed with the Securities and Exchange Commission (the "SEC") and in any subsequent periodic or current report that the Company files with the SEC. All forward-looking statements reflect the Company's estimates only as of the date of this release (unless another date is indicated) and should not be relied upon as reflecting the Company's views, expectations, or beliefs at any date subsequent to the date of this release. While Fusion may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so, even if the Company's estimates change.

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