Jazz Pharmaceuticals Presents Pre-Clinical Data for Pan-RAF Inhibitor JZP815, including Pharmacokinetic Properties and Efficacy in Multiple Solid Tumor Types

April 8, 2022

Novel, investigational drug JZP815 inhibited tumor growth in several RAS- and BRAF-mutated solid tumor models, and demonstrated enhanced activity when combined with other MAPK pathway inhibitors

Jazz plans to submit an investigational new drug application (IND) for JZP815 this year

DUBLIN, April 8, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) and collaboration partner Redx Pharma (AIM: REDX) today presented data showing the pan-RAF kinase inhibitor, JZP815, was active in multiple RAF- and RAS-mutant tumor pre-clinical models, with a pharmacokinetic profile that may provide drug exposure required for target engagement in humans.

"As a precision pan-RAF inhibitor with a differentiated mechanism of action, JZP815 is a promising drug candidate for several types of difficult-to-treat solid tumors, including colorectal cancer, non-small cell lung cancer, melanoma and ovarian cancer," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "By not inducing paradoxical pathway activation, which can stimulate the growth of certain cancers, JZP815 may offer a significant advancement in the pan-RAF inhibitor class with the potential to address unmet patient need. We look forward to submitting the investigational new drug application for JZP815 this year."

JZP815 targets specific components of the mitogen-activated protein kinase (MAPK) pathway, namely all three RAF proteins – ARAF, BRAF and CRAF – that when activated by oncogenic mutations, can be a frequent driver of human cancer.

Pre-clinical data of JZP815 administered orally as both a monotherapy and in combination with mitogen-activated protein kinase (MAPK) pathway inhibitors were presented at the American Association for Cancer Research 2022 Annual Meeting (AACR). Key findings of several pre-clinical models include[1]:

- JZP815 inhibited all 3 RAF kinase family members (ARAF, BRAF, CRAF) at low-to-sub nanomolar potencies in biochemical assays.
- JZP815 did not induce significant paradoxical pathway activation, observed with approved first generation BRAF-selective inhibitors, while demonstrating equivalent cellular potencies for MAPK pathway inhibition driven by either mutant RAF monomers or dimers or mutant RAS-induced RAF dimers in tumor cells.
- JZP815 significantly inhibited tumor growth, including inducing tumor regression, as a single agent in multiple mouse xenograft solid tumor models harboring RAS and/or BRAF mutations.
- JZP815's pharmacokinetic profile sustained on-target pathway pharmacodynamic responses in a predictable dose and time dependent manner.
- JZP815 demonstrated enhanced activity when combined with inhibitors of other MAPK pathway components including MEK1/2, SOS1, SHP2 and EGFR inhibitors in both class 2 and class 3 mutant BRAF patient-derived tumor cells *ex vivo*, and KRAS mutant NSCLC and colorectal cancer xenografts *in vivo*.

The full Jazz presentation abstract, titled, "JZP815, a potent and selective pan-RAF inhibitor, demonstrates efficacy in RAF and RAS mutant tumor pre-clinical models" is available at https://www.abstractsonline.com/pp8/#!/10517/presentation/15283.

Jazz acquired JZP815 from Redx Pharma, and the two companies are collaborating on this pre-clinical research. Jazz plans to submit an IND for JZP815 this year.

About JZP815

JZP815 is an investigational, pre-clinical stage pan-RAF kinase inhibitor that was discovered and developed using state-of-the-art screening methodologies and medicinal chemistry. JZP815 targets specific components of the mitogen-activated protein kinase (MAPK) pathway that, when activated by oncogenic mutations, can be a frequent driver of human cancer. JZP815 potently inhibits both monomer- and dimer-driven RAF signaling (e.g., RAS-induced), prevents paradoxical pathway activation induced by BRAF selective inhibition, and is active against class 1, class 2, and class 3 BRAF mutants, as well as BRAF fusions and CRAF mutants. JZP815 is not currently approved for use anywhere in the world. JZP815 is part of Jazz's growing early-stage R&D pipeline focused on precision oncology in solid tumors.

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (NASDAQ: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases—often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

Caution Concerning Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' belief in the potential of JZP815 to provide a potentially new therapeutic option for multiple solid tumor types; progressing JZP815 to the clinic and other statements that are

not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, effectively registering JZP815 with FDA and initiating clinical trials; launching and commercializing new products; obtaining and maintaining adequate coverage and reimbursement for the company's products; delays or problems in the supply or manufacture of the company's products; and other risks and uncertainties affecting the company, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals' Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2021 and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

Media Contact:
Kristin Bhavnani
Head of Global Corporate Communications
Jazz Pharmaceuticals plc
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Investors:
Andrea N. Flynn, Ph.D.
Vice President, Head, Investor Relations
Jazz Pharmaceuticals plc
investorinfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

References

[1] Hauptschein, R. et al. JZP815, a potent and selective pan-RAF inhibitor, demonstrates efficacy in RAF and RAS mutant tumor pre-clinical models. American Association for Cancer Research 2022 Annual Meeting. Available at www.abstractsonline.com/pp8/#!/10517/presentation/15283. Accessed April 2022.

View original content to download multimedia:https://www.prnewswire.com/news-releases/jazz-pharmaceuticals-presents-pre-clinical-data-for-pan-raf-inhibitor-jzp815-including-pharmacokinetic-properties-and-efficacy-in-multiple-solid-tumor-types-301520973.html

SOURCE Jazz Pharmaceuticals plc