



DPP8/9 Inhibition - The Primary Mechanism of BioXcel Therapeutics' Lead Immuno-Oncology Asset, BXCL701, Highlighted in Peer-Reviewed Journal

July 24, 2018

Nature Medicine article expands upon mechanistic findings and presents DPP8/9 inhibition as potential treatment for various cancer types

BXCL701 being developed for two rare malignancies: pancreatic cancer and treatment emergent neuroendocrine prostate cancer (tNEPC)

NEW HAVEN, Conn., July 24, 2018 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. ("BTI") (Nasdaq:BTAI), is a clinical stage biopharmaceutical development company utilizing proprietary artificial intelligence approaches to identify the next wave of medicines across neuroscience and immuno-oncology, today announced that dipeptidyl peptidase (DPP) 8/9 inhibition, the primary mechanism of action of its lead immuno-oncology candidate, BXCL701, was highlighted in an article in the July 2018 edition of the peer-reviewed journal *Nature Medicine*.

BXCL701 is a potential first-in-class, highly potent oral small molecule immuno-modulator that has demonstrated single agent activity in melanoma, with an established safety profile from 700 healthy subjects and cancer patients. It is designed to stimulate both the innate and acquired immune systems by inhibiting DPP8/9 and blocking immune evasion by inhibiting Fibroblast Activation Protein (FAP).

The paper titled "[DPP8/DPP9 inhibitor-induced pyroptosis for treatment of acute myeloid leukemia](#)" by Darren C. Johnson, et al., concluded that activation of caspase recruitment domain-containing protein 8 (CARD8) acts as an inflammasome sensor to activate caspase-1 and mediates DPP8/9 inhibitor-induced cell death in myeloid cells¹. This therapeutic strategy serves as a potential pathway for direct cytotoxicity of acute myeloid leukemia (AML) cells and indirect response to solid tumors. Multiple prior studies have established DPP8/9 as a novel immune checkpoint that controls the activation of the innate immune system^{2,3}.

"BXCL701 is novel in its ability to stimulate both the innate and acquired immune systems by inhibiting DPP8/9 and blocking immune evasion by inhibiting FAP," said Vimal Mehta, PhD, Chief Executive Officer of BTI. "This publication highlights one component of BXCL701's dual mechanism of action, providing valuable insights on the effects of DPP8/9 inhibition. BXCL701 differentiates itself by activating the innate immune system and stimulating neutrophils, natural killer cells and effector T cells. The paper provides further mechanistic understanding of DPP8/9 inhibition and validates its importance as a promising therapeutic approach, not only for solid tumors but for hematologic malignancies as well."

BTI expects to initiate Phase 2 proof of concept studies evaluating BXCL701 in pancreatic cancer and tNEPC later this year. BTI is also evaluating BXCL701's potential in additional indications, both as a monotherapy and in combination with other immuno-oncology agents and partnering strategies.

Vincent J. O'Neill, MD, Chief Medical Officer of BTI added, "BXCL701 has generated compelling preclinical data in pancreatic cancer and a variety of other tumor models. Particularly exciting is its ability to block immune evasion and aid in the formation of memory T-cells, which may support long-term immunity in certain types of cancer as presented by BTI at ASCO 2018⁴."

This study in AML led by Dr. Bachovchin's team at the Memorial Sloan Kettering Cancer Center and the Weil Cornell Graduate School of Medical Sciences, demonstrates that the therapeutic potential of a DPP8/9 inhibitor such as BXCL701 can extend beyond solid tumors into hematologic malignancies.

Dr. O'Neill concluded, "We look forward to further evaluating BXCL701 in our lead indications, and potentially expanding its application to other cancer types."

1. Johnson, DC, et al. DPP8/DPP9 inhibitor-induced pyroptosis for treatment of acute myeloid leukemia." *Nat Med* (2018), PMID: 29967349; DOI:10.1038/s41591-018-0082-y
2. Okondo, Marian C., et al. "DPP8 and DPP9 inhibition induces pro-caspase-1-dependent monocyte and macrophage pyroptosis." *Nat Chem Biol* 13.1 (2017): 46-53. PMID: 27820798; DOI:10.1038/nchembio.2229
3. Okondo, Marian C., et al. "Inhibition of Dpp8/9 activates the Nlrp1b inflammasome." *Cell Chem Biol* 25.3 (2018): 262-267. PMID: 29396289; DOI:10.1016/j.chembiol.2017.12.013
4. Rastelli et al., Presented at ASCO 2018, Illinois, [Abstract #3085](#)

About BioXcel Therapeutics, Inc. (BTI):

BioXcel Therapeutics, Inc. is engaged in the development and advancement of the next wave of medicines, initially targeting the treatments in oncology and CNS diseases. The company's lead therapeutic candidates are BXCL701, a DPP8-9/FAP inhibitor with broad potential application in oncology indications, both as a monotherapy and in combination with immuno-oncology agents, and BXCL501, a proprietary sublingual formulation of an anesthetic for the treatment of acute agitation, with the potential to expand into other neuropsychiatric and neurodegenerative disorders. The company's strategy is to apply a drug re-innovation approach to develop therapeutic candidates with a high probability of clinical and regulatory success. For more information, please visit www.bioxceltherapeutics.com.

Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements in this press release include, but are not limited to, statements that relate to the advancement and development of BXCL701, the

commencement of clinical trials, the availability of data from clinical trials and other information that is not historical information. When used herein, words such as “anticipate”, “being”, “will”, “plan”, “may”, “continue”, and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon BioXcel’s current expectations and various assumptions. BioXcel believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. BioXcel may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important factors, including, without limitation, market conditions and the factors described under the caption “Risk Factors” in BioXcel’s prospectus dated March 7, 2018, and BioXcel’s other filings made with the Securities and Exchange Commission. Consequently, forward-looking statements should be regarded solely as BioXcel’s current plans, estimates and beliefs. Investors should not place undue reliance on forward-looking statements. BioXcel cannot guarantee future results, events, levels of activity, performance or achievements. BioXcel does not undertake and specifically declines any obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances or to reflect the occurrences of unanticipated events, except as may be required by law.

Contact Information:

The Ruth Group for BioXcel:

Lee Roth / Janhavi Mohite

646-536-7012 / 7026

lroth@theruthgroup.com / jmohite@theruthgroup.com

Source: BioXcel Therapeutics, Inc.