



## **Accent Therapeutics Presents Data Supporting DHX9 Inhibition as a Novel Therapeutic Modality at American Association for Cancer Research (AACR) Annual Meeting 2023**

*Data support DHX9 inhibition as a novel therapeutic modality in microsatellite instable colorectal cancer and describe the first identification of potent and selective small molecule inhibitors of DHX9*

*Proprietary crystal structures of DHX9 enable rapid, structure-based drug discovery for novel oncology target*

**LEXINGTON, Mass., April 16, 2023** – Accent Therapeutics, a biopharmaceutical company developing breakthrough, oncology-focused small molecule therapies that target RNA-modifying proteins (RMPs), today presented data supporting DHX9 inhibition as a novel cancer treatment approach at the American Association for Cancer Research (AACR) Annual Meeting 2023 in Orlando, Florida.

DHX9 is a multifunctional DEAH-box RNA helicase which has been reported to play important roles in replication, transcription, translation, and RNA splicing – critical processes that contribute to maintenance of genomic stability. Microsatellite instable (MSI) tumors exhibiting defective mismatch repair (dMMR) show a strong dependence on DHX9, making the helicase an attractive target for oncology drug discovery.

“Accent is advancing the compelling and growing body of evidence linking RMPs to cancer pathobiology and demonstrating their untapped potential for addressing cancers with high unmet clinical need. Our systematic analysis of the RMP landscape has revealed several promising precision oncology targets, including DHX9. The data presented at AACR illustrate strong proof-of-concept supporting DHX9 inhibition as a promising approach to addressing MSI tumors and validate the overall utility of RMPs as a compelling target class for oncology drug development,” said Robert A. Copeland, Ph.D., President, Founder, and Chief Scientific Officer of Accent Therapeutics. “We are pleased with our rapid progress advancing from target identification to promising therapeutic programs and look forward to bringing these therapies closer to patients.”

The data presented at the meeting provide compelling support for targeted inhibition of DHX9 as a novel therapeutic modality in MSI colorectal cancer (CRC) and describe the first identification of potent and selective small molecule inhibitors of DHX9 that demonstrate tumor cell killing in both *in vitro* and *in vivo* preclinical cancer models.



Informed by a proprietary crystal structure of human DHX9, Accent used structural considerations to design selective small molecule inhibitors of the protein and developed a robust assay suite to characterize inhibitor activity. Data from xenograft models demonstrate that oral administration of one such compound, ATX968, was well tolerated *in vivo* and induced durable tumor regression during the 28-day treatment period, with minimal tumor regrowth observed within a 28-day post treatment window. Dose dependent changes in biomarkers of DHX9 inhibition, such as circular RNA induction – which can be measured in peripheral blood, indicate a promising pharmacokinetic (PK)/pharmacodynamic (PD) profile and further validate DHX9 as a promising new oncology target.

“Our DHX9 program is one in a portfolio of high impact, RNA-modifying targets that Accent is pursuing with novel, oncology-focused small molecules,” said Shakti Narayan, Ph.D., J.D., Chief Executive Officer of Accent. “This progress is a testament to our team’s ability to leverage deep insights into cancer biology and structure-based drug development to deliver new precision oncology therapies with transformative potential.”

The abstract is available online as part of the annual meeting’s *Proceedings* supplement in AACR’s journal, *Cancer Research*, and the presentation will be archived on the Accent Therapeutics website, [www.accenttx.com](http://www.accenttx.com).

**Presentation details are as follows:**

**Title:** [Targeting DHX9 Inhibition as a Novel Therapeutic Modality in Microsatellite Instable Colorectal Cancer](#)

**Authors:** *Jennifer Castro, Matthew H. Daniels, Chuang Lu, David Brennan, Deepali Gotur, Young-Tae Lee, Kevin Knockenhauer, April Case, Jie Wu, Shane M. Buker, Julie Liu, Brian A. Sparling, E. Allen Sickmier, Stephen J. Blakemore, P. Ann Boriack-Sjodin, Kenneth W. Duncan, Scott Ribich, Robert A. Copeland*  
Accent Therapeutics, Lexington, MA

**Abstract Number:** 1136

**Session Category:** Experimental and Molecular Therapeutics

**Session Title:** Innovative Therapeutic Approaches

**Session Date and Time:** Sunday, April 16, 2023 3:00 – 5:00 PM ET

**Session Location:** Room W331, Orange County Convention Center, Orlando, Florida

**About DHX9**

DHX9 is a multifunctional DEAH-box RNA helicase which has been reported to play important roles in replication, transcription, translation, RNA splicing and RNA processing which contribute to DHX9’s role in maintenance of genomic stability. Overexpression of DHX9 has been observed in multiple cancer



types, including colorectal cancer (CRC). In addition, microsatellite instable (MSI) tumors exhibiting defective mismatch repair (dMMR) show a strong dependence on DHX9, making this helicase an attractive target for oncology drug discovery.

#### **About Accent Therapeutics**

Accent Therapeutics is a biopharmaceutical company developing breakthrough, oncology-focused small molecule therapies by targeting key RNA-modifying proteins (RMPs). This field of biology encompasses post-transcriptional chemical modifications of RNA that provide cells with a unique mechanism for regulating proteins critical for cellular growth and differentiation. By targeting cancer-linked RMPs with precision therapies, the Company aims to translate extraordinary science into life-changing therapies for patients. For more information, please visit [www.accenttx.com](http://www.accenttx.com) or follow us on [LinkedIn](#).

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