Discovered by AI

Dr. Vimal Mehta, CEO of BioXcel Therapeutics, talks about the company's clinical candidates identified through an artificial intelligence and machine-learning platform.

BioXcel Therapeutics is showing that investments in artificial intelligence (AI) and machine learning can pay off. The company is using AI to identify the next wave of medicines across neuroscience and immuno-oncology. The company's approach leverages existing approved drugs and/or clinically validated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indices. BioXcel Therapeutics, one of the first companies to publicly identify candidates discovered through AI processes, is currently moving forward two drug candidates in clinical development.

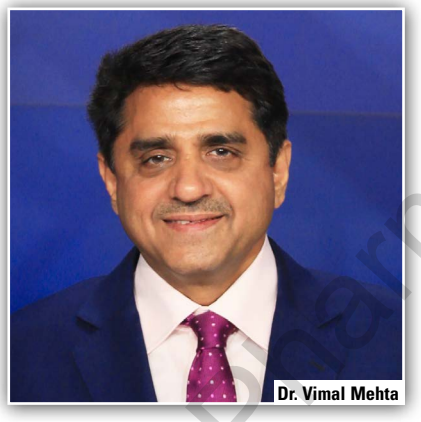
One candidate is BXCL701, a first-in-class DPP8/9 and FAP inhibitor, currently being developed for the treatment of pancreatic and treatment emergent neuroendocrine prostate cancer (tNEPC). A second product is BXCL501, a sublingual thin film formulation of dexmedetomidine, or Dex, which is designed for acute treatment of agitation resulting from neurological and psychiatric disorders.

"We use a proprietary artificial intelligence platform to identify potential drug candidates," says Vimal Mehta, Ph.D., CEO and founder of BioXcel Therapeutics. "Once we have identified the opportunity, our discovery team and translational team works to validate that what we identified makes sense in terms of the models and translational work."

One advantage of this approach is the reduced time required for choosing product candidates. "We don't need five or six years of lead time to develop a Phase II compound because we are only working on potential drugs that have already been tested in humans," he explains. "We believe we can be in the clinic in nine or 12 months using our approach."

Other advantages include an increased probability of success and lowered costs related to R&D.

"More than 5,000 publications come out every day," he says. "There are 50 million or so publications and materials related to every level of clinical trial information. It's impossible for anybody to keep up on all that information. Data are doubling every few years. We have no choice: at some point, we have to use technology."



Dr. Vimal Mehta

Dr. Mehta, however, stresses it takes an integrative approach to make AI and machine learning applicable to drug discovery.

"Using AI we can crunch data from millions of publications," he says. "But once such large amounts of data are crunched, there can also be a lot of noise. Our expertise with the proprietary algorithms and the deep domain expertise help us figure out where the real opportunity is in terms of a drug candidate. That's why we say integration of artificial intelligence platforms with real developmental expertise is a key for success."

He says there is no magic button when using AI. "The process requires understanding what you want to feed into the machine, how you want to train your machine, and how you interpret what comes out of the machine," Dr. Mehta says. "Our lesson is that there is a level of expertise needed to use AI to identify opportunities."

A second lesson, he says, is you have to continually fine-tune the process. "Humans learn from the machines, and machines learn from humans."

Going forward, BioXcel Therapeutics will continue to look for new opportunities while conducting clinical development of its two lead product candidates. The company plans to initiate Phase II trials in the second half of 2018 for BXCL701 for prostate cancer as a monotherapy and in combination with immune-checkpoint inhibitors.

BXCL701 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). It represents a novel, and highly attractive approach to the modulation of the tumor microenvironment needed to switch "cold" tumors into "hot" immune-permissive tumors.

The therapy was initially being evaluated in neuroendocrine prostate cancer and pancreatic cancer in a research partnership with Nektar. It has demonstrated single-agent activity in melanoma, with an established safety profile from 700 healthy subjects and cancer patients.

"We are targeting two rare forms of the tumor," Dr. Mehta says. "One is in the area of pancreatic cancer and the second one is in the area of NEPC. We are focusing on these two cancers because currently there's no standard of care, and there is a very high unmet medical need."

In animal studies, BXCL701 produced a complete regression of tumors, he says. "Neither of the single agents nor the double agents produced this type of a response," Dr. Mehta explains. "We also confirmed that this creates a vaccine-like response."

BioXcel Therapeutics' second candidate is BXCL501, a sublingual thin film formation of Dex for acute treatment of agitation resulting from neurological and psychiatric disorders. The product is in Phase Ib trials.

In June 2018, the company announced positive data from its Phase Ib study evaluating intravenous (IV) administration of Dex. Data from this study will aid in establishing the optimal dose for BXCL501 for the acute treatment of agitation. The study enrolled 16 healthy volunteers 55 to 75 years of age. The primary endpoint of the study was the dose and drug exposure levels required to produce mild sedation, which can serve as a surrogate endpoint for treating agitation using the Richmond Agitation-Sedation Scale (RASS)2 score.

Treatment of agitation remains a significant global healthcare challenge in patients with various neuropsychiatric disorders and dementia, as the currently available treatment options are suboptimal, invasive, and difficult-to-administer. PV

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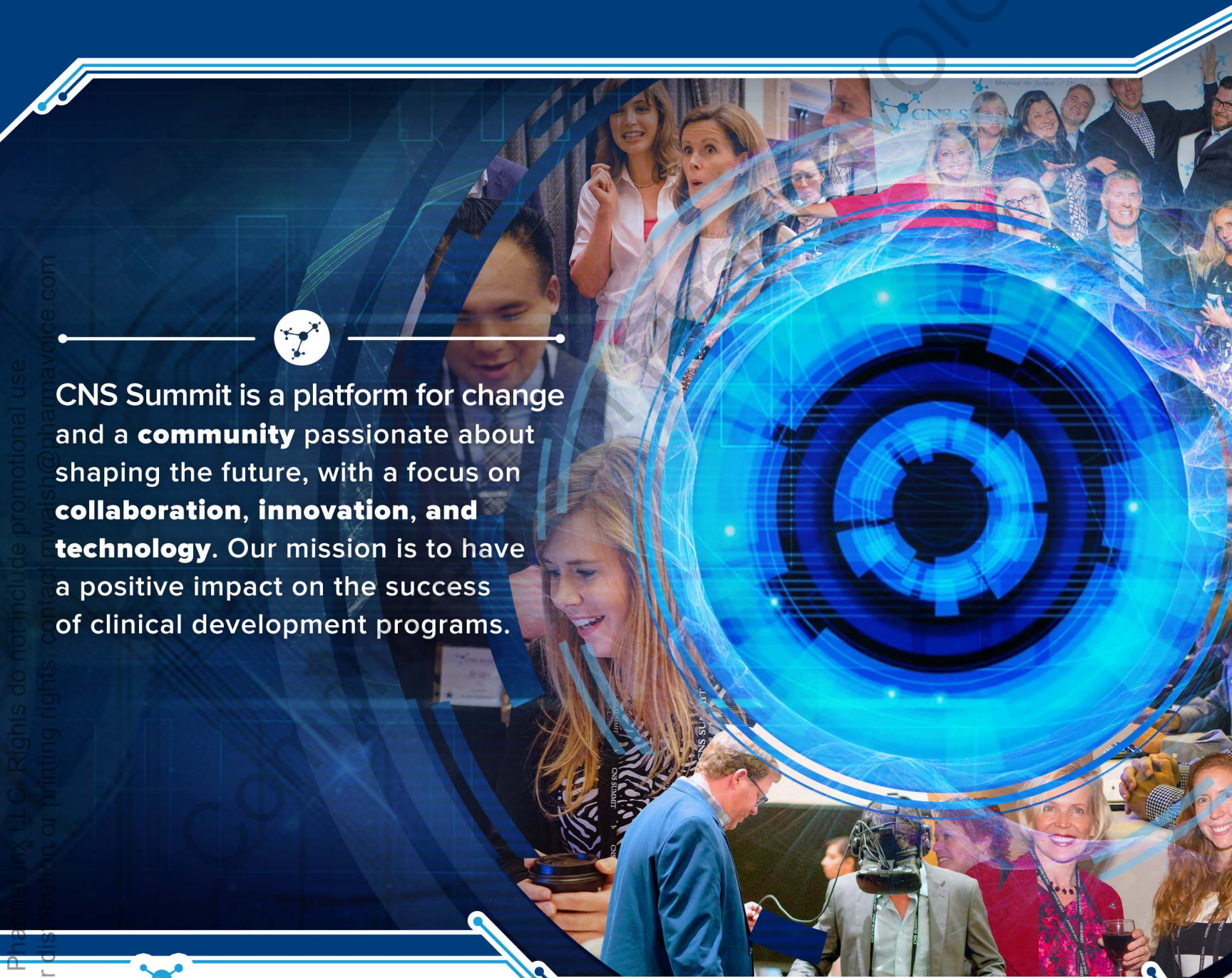

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