Combination of Checkpoint Inhibitors and Intezyne's Novel Cancer Resistance Pathway Inhibitor IT-139 Shows Enhanced Immune Efficacy

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Intezyne Technologies, Inc.

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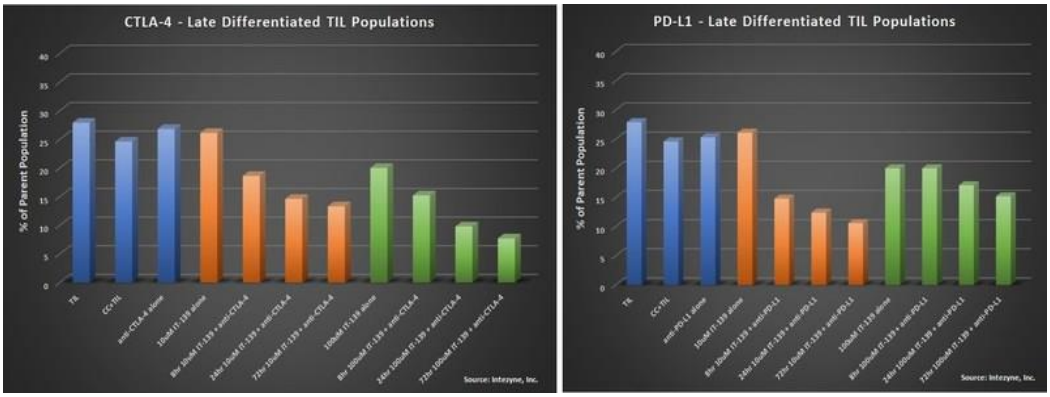
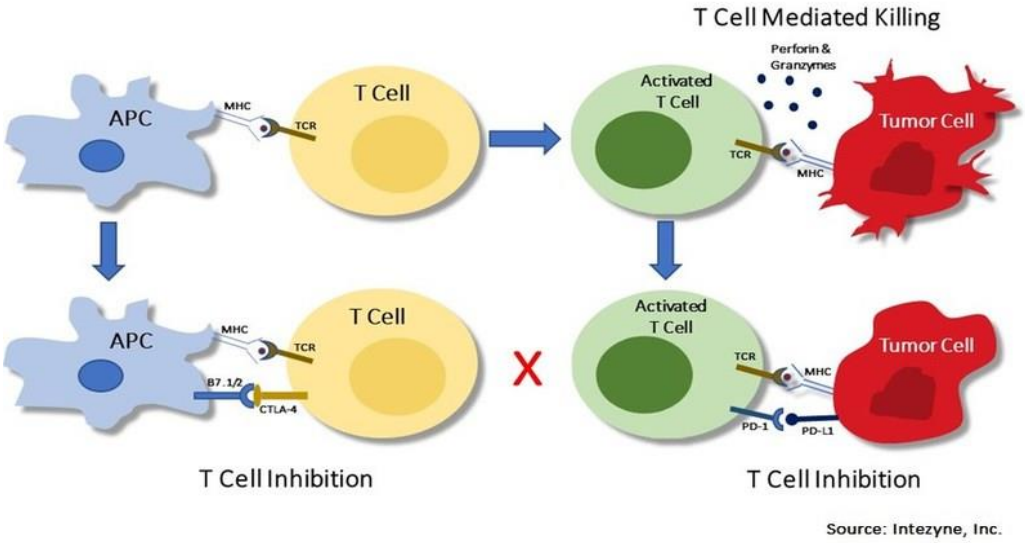
TAMPA, Fla., April 10, 2018 /PRNewswire/ -- Intezyne, a clinical-stage biopharmaceutical company developing novel anti-cancer therapies, announced exciting results from their ongoing preclinical studies of novel cancer resistance pathway inhibitor IT-139 in combination with immune checkpoint inhibitor molecules such as anti-PD-L1 and anti-CTLA-4, with IT-139's effect on reducing checkpoint blockade resistance showing enhanced immune efficacy in vivo. As a result, Intezyne anticipates exploring therapeutic combinations with existing and development-stage checkpoint inhibitors.



Combinations with IT-139 favor early differentiation in TILs when compared to immune checkpoint monotherapy.



T Cell Mediated Killing

Intezyne's immune blockade combination studies draw on the premise that T cells are profoundly affected by stress, primarily due to increased protein synthesis, as more than 100 newly synthesized proteins are present on T cells under stress. This increased level of protein synthesis and folding required by activated, effector human T cells, which pack most of the punch when it comes to anti-tumor effects, lead to an exhausted and dysfunctional population of cells that have reduced efficacy against tumors. These weak cells often express increasingly high levels of inhibitory receptors including PD-L1 and CTLA-4. Intezyne's research goal is to provide insight into the molecular mechanisms of immune checkpoint inhibitor resistance which is critical to develop combinatorial drug therapy to potentiate therapeutic responsiveness.

GRP78 is the master regulator of the Unfolded Protein Response (UPR), and recent studies have shown that components of the UPR are upregulated after the development of checkpoint therapy resistance compared to before treatment. These findings indicate that UPR signaling may play a novel role in checkpoint inhibitor therapy resistance. Upregulated UPR signaling has also been shown to promote T cell dysfunction, which prevents immune-mediated cancer cell killing as well.

In the 2017 Annual AACR Meeting, the first symposium session for GRP78 and the UPR was held. The key speaker was Dr. Amy Lee from the Norris Cancer Center at USC, who presented her data showing IT-139's effect on GRP78. Dr. Lee's 2013 Oncogene article is recognized as one of their most highly cited papers, reflecting the growing interest in GRP78 and the UPR as important targets for cancer treatment. IT-139 is the only small molecule in clinical trials that targets GRP78. Additional data on IT-139 will be presented at the upcoming 2018 Annual AACR Meeting.

In vitro studies at Intezyne have shown increased anti-tumor effect and down regulation of GRP78, and by extension, the UPR and its pro-tumor effects, thus shifting the immune cell

populations from exhausted and senescent towards non-exhausted and increasingly potent effector T cells.

For more information, please visit the Company's website at www.intezyne.com.

Contact:
E. Russell McAllister, CEO
193110@email4pr.com, (813) 609-5017

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