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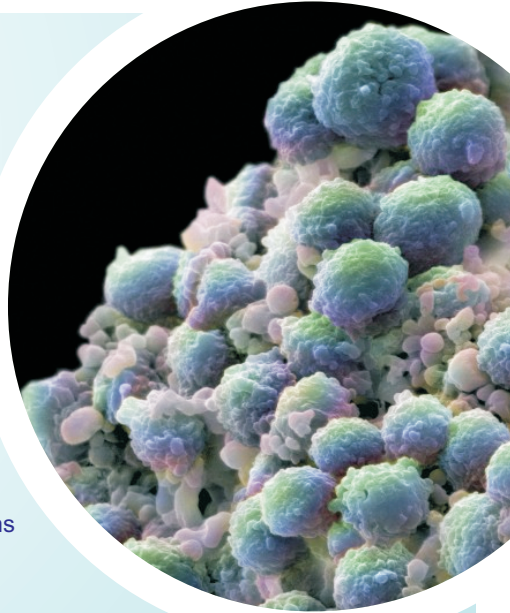
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**Ascenta Therapeutics, Inc.** is a privately-held, clinical-stage biopharmaceutical company that discovers and develops new medicines for the treatment of cancer.

Licensed from both the National Institutes of Health and the laboratory of Dr. Shaomeng Wang at the University of Michigan, Ascenta's technology is focused on discovering molecules that target proteins responsible for prolonging cancer cell survival.

## Scientific Approach FINDING KEYS TO UNLOCK APOPTOSIS

Multicellular organisms use apoptosis, or programmed cell death, to eliminate abnormal or unwanted cells. As a result of accumulated mutations, all cancer cells fail to execute an apoptotic program, allowing them to live indefinitely and grow uncontrollably. In fact, the breakdown of the cellular apoptosis regulatory machinery is a hallmark of cancer. Most current cancer therapies, including chemotherapeutic agents, radiation, and immunotherapy, work by inducing apoptosis in cancer cells. However, because the normal apoptotic pathways are defective, many cancer cells are resistant or develop resistance to these agents. Accordingly, a promising new direction for drug development involves targeting apoptotic proteins directly to induce cell death and/or reduce resistance to other treatments.

Ascenta's pipeline now includes several potential anticancer therapies that target different parts of the apoptotic pathway to inhibit the proliferation of abnormal cells and reestablish the cell death program (pipeline details on reverse page).

DISCOVERY	PRECLINICAL	PHASE I		PHASE II		PHASE III
		IND		Exploratory	Confirmatory	NDA
<b>AT-101: Oral pan-Bcl-2 Inhibitor</b>						
Prostate (HRPC-1L) Taxotere®-Eligible Patients						With Taxotere®
Prostate (HRPC-2L) Taxotere®-Refractory Patients						With Taxotere®
Lung (NSCLC-2L) Taxotere®-Eligible Patients						With Taxotere®
Lung (SCLC) 1st & 2nd-line Chemo combinations						
Glioma (GBM) with Radiation & Chemotherapy						
B-Cell Malignancies (NHL & CLL) with Chemo/Biologics						
Prostate (HSPC) Hormone-Sensitive Patients						
Esophageal with Radiation & Chemotherapy						
<b>AT-406: Oral multi-IAP Inhibitor</b>						
Solid Tumors, Lymphoma, and Leukemia						
<b>Oral Inhibitor of HDM2-p53</b>						
Cancers						

### Investors

Ascenta's investors include Domain Associates, Enterprise Partners, Pac-Link, Perseus LLC, Scale Venture Partners, Sofinnova Ventures, and US Venture Partners.





### **AT-101: Pan-Bcl-2 Inhibitor**

AT-101 is an orally-active, pan-Bcl-2 inhibitor (including Bcl-2, Bcl-xL, Bcl-w, and Mcl-1 inhibition) that has been shown to induce apoptosis directly by operating as a BH3 mimetic and indirectly as an independent upregulator of Noxa and Puma. By blocking the binding of Bcl-2 family members with proapoptotic proteins and upregulating specific proapoptotic factors, AT-101 lowers the threshold for cancer cells to undergo apoptosis in various tumor types.

In Phase I and Phase II trials, AT-101 has demonstrated single-agent cytoreductive activity in several cancers, including chronic lymphocytic leukemia (CLL), non-Hodgkins lymphoma (NHL), and prostate cancer. Phase II combination trials are ongoing in several cancers, including hormone-refractory prostate cancer and non-small cell lung cancer (with Taxotere<sup>®</sup>), B-cell malignancies (with Rituxan<sup>®</sup>), small cell lung cancer (with Hycamtin<sup>®</sup>), glioma (with Temodar<sup>®</sup>, +/- chemoradiotherapy [XRT]) and esophageal cancer (with docetaxel, 5-fluorouracil and XRT). Initial findings from an ongoing open-label, multi-center study of AT-101 in combination with docetaxel and prednisone in patients with hormone-refractory prostate cancer (HRPC) demonstrated that AT-101 can be safely administered and produces clinical responses, based on both PSA and tumor shrinkage (RECIST) criteria.

### **AT-406: Multi-IAP Inhibitor**

AT-406 is an orally-active, small molecule drug designed to promote programmed cell death (apoptosis) in tumor cells by blocking the activity of "inhibitors of apoptosis proteins" or IAPs (including XIAP, c-IAP1, c-IAP2, and ML-IAP) to create conditions in which apoptosis can proceed. As such, AT-406 is considered a multi-IAP antagonist. IAPs are key components of the complex cascade of protein signaling that activates enzymes called caspases to initiate the breakdown of the cancer cell. AT-406 is thought to mimic the activity of Smac (second mitochondria-derived activator of caspases) by binding to XIAP and preventing it from inhibiting caspase activation. Upon binding to cIAP1 and cIAP2, AT-406 induces rapid degradation of these proteins and promotes apoptosis through activation of the death-receptor complex and caspase 8.

AT-406 has demonstrated strong single-agent antitumor activity in multiple xenograft models of human cancer, including breast cancer, pancreatic cancer, prostate cancer, and lung cancer. AT-406 has also been shown to work synergistically with conventional chemotherapeutic and targeted agents (such as TRAIL and tyrosine kinase inhibitors) in preclinical tumor models. Recently, AT-406 received approval by the U.S. Food and Drug Administration (FDA) of its Investigational New Drug (IND) Application and clinical trials will be initiated during the fourth quarter of 2009.

### **HDM2 Inhibitor**

Ascenta's third program involves inhibition of HDM2 (Human Double Minute 2), a protein that regulates the activity of another important component of the apoptotic pathway, the p53 tumor suppressor protein. Ascenta has a potent, non-peptide small molecule that restores p53 function in cancer cells with wild-type (unmutated) p53. This orally-active agent is in late-stage preclinical development.



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