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ONCOLOGY BUSINESS REVIEW

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AND SENIOR VICE PRESIDENT, R&D, KENNETH BAIR, AND MORE...**

Interview with Entremed, Inc. President & CEO, James S. Burns, and Senior Vice President, R&D, Kenneth Bair

Entremed, Inc. (Nasdaq: ENMD) is a clinical-stage pharmaceutical company that focuses on angiogenesis, cell cycle regulation, and inflammation—processes that are vital to the progression of cancer and other diseases.

Entremed's three main product candidates, include:

- MKC-1, a novel cell cycle inhibitor currently in six clinical trials: a Phase 2 trial in patients with metastatic breast cancer, a Phase 2 trial in pancreatic cancer, a Phase 2 trial in ovarian/endometrial cancers, a Phase 1 study for hematologic cancers, a Phase 1/2 study in combination with pemetrexed (Alimta®) in patients with NSCLC, and most recently, a Phase 1 continuous dosing study in advanced cancer.
- ENMD-1198, an orally-active, antimetabolic agent that causes cell cycle arrest and apoptosis in tumor cells, is in a Phase 1 study for patients with solid tumors.

- ENMD-2076, a selective kinase inhibitor with potent activity against Aurora A and tyrosine kinases linked to promoting cancer and inflammatory diseases, is expected to commence a Phase 1 study for solid tumors in April '08 and a Phase 1 study for hematological tumors the third or fourth quarter of '08.

Entremed has limited its expenditures on Panzem® NCD (2-methoxyestradiol or 2ME2) for oncology in order to progress with the three oncology programs noted above; however, the company plans to move Panzem® forward in rheumatoid arthritis (RA) with the recent acceptance of the IND.

Recently, OBR conducted an interview with Entremed's management team: James S. Burns, President & CEO and Kenneth Bair, Ph.D., Senior Vice President, R&D. Following is an excerpt discussing the company's business strategy and its core scientific strengths.



James S. Burns,
President & CEO, Entremed

its core scientific expertise in small molecules that have both antiproliferative and antiangiogenic properties. ENMD-1198 and ENMD-2076 were both discovered internally. MKC-1 is licensed from Roche, through our acquisition of Miikana Therapeutics.

OBR: *What can you tell us about Entremed's core strategy and products?*

JB: Ours is a rebuild story that has a purposeful strategy. Our strategy has been to bulk up our pipeline with multiple Phase 1 and Phase 2 compounds that will provide us with more than one opportunity to be successful, but at the same time we want to mitigate some of the downside risks associated with oncology drug development. We have rebuilt the company around

OBR: *How are you accomplishing your goals?*

JB: We had to get the company very focused on making the conversion to oncology clinical development. We had an excellent core team that could take compounds from research, through preclinical work, and into the early stages of clinical development; what we needed was a big pharma perspective to guide our research efforts and to align our partnering efforts with big pharma expectations. We brought in Ken Bair to help us transition into a later stage clinical company.

KB: Another key aspect in our transition is pipeline management. With a burgeoning pipeline, we have had to make hard but necessary decisions to drop projects so we could focus our resources on fewer programs with greater potential.

OBR: *Of course the problem with a burgeoning pipeline is the expense associated with it. Are you feeling like you're well-funded to support a streamlined but still robust pipeline?*



JB: We have enough cash to take us well into '09. From a cash utilization perspective, we keep performing consistently better than we set out to; we're very tight on cash management.

OBR: *One could argue that a measure of success for a mid-stage company is the ability to partner. Are you actively looking to secure partnerships?*

JB: We've already started looking for partners for our selective kinase inhibitor, ENMD-2076. However, we were probably a little too ambitious with it because what potential partners wanted to see in this particular compound was its toxicity profile in animal models. We have that data now so it's time to go back and talk to them.

We have full worldwide commercial rights to all of our product candidates. We also have strong intellectual property protection (including composition of matter) for all of our compounds, which are backed by solid preclinical data packages that provide an informed direction for our clinical development efforts. We will pursue development and/or out-licensing partners to help accelerate development, offset the cost of larger clinical trials, and strengthen our own development capabilities. In addition to ENMD-2076, we are seeking partnership opportunities for MKC-1 for oncology and Panzem® for RA.

OBR: *Why is ENMD-2076 the one you're choosing to partner first?*

KB: Because it is a hot area. The larger drug companies are now very sophisticated in their understanding of kinases and their relevance in vitro and in vivo. We have animal data on ENMD-2076 and as we move into human clinical trials this year, we'll be looking at tissue samples in patients before, during, and after therapy to get information on how the compound is working. We also think the product has a solid safety profile. Given these properties, we think we have a strong anti-cancer product which will be attractive to larger companies interested in partnering with us.

JB: We're trying to be both opportunistic and strategic about partnering. We hope that partnering will allow us to continue developing the other compounds that we have on the oncology track and continue to create shareholder value.

OBR: *Please tell us about the clinical trial development of your other lead compounds, MKC-1 and ENMD-1198.*

JB: MKC-1 arrests cellular mitosis and induces cell death inhibiting PI3K-Akt-mTOR and members of the importin beta family. The Phase 1 study of ENMD-1198 has proceeded through multiple cohorts without any drug-related toxicity at doses that are approaching the maximum tolerated dose in preclinical models. We expect to complete this study around mid-year with additional trials expected in the second half of '08.

In addition, we are planning to move Panzem® (2ME2) forward into early RA clinical trials and seek a partner for later stage studies. Based on Panzem's demonstrated safety profile and activity in RA models, we believe it represents a "first-in-class" opportunity for an oral DMARD compound in a large multi-billion dollar global market.

OBR: *You paint a colorful picture of your product candidates and potentials. What is your explanation for the share price not moving?*

JB: Most oncology companies at Phase 1 and the early part of Phase 2 trials are suffering from similar lagging share prices and, if you look across the board, our class of companies has lost a lot of market capitalization. Our near term concern is making sure we have the cash to fund the research programs that we have. We ended 2007 with sufficient cash resources to take us well into 2009. In our business, like any other, if we pay attention to the fundamentals and follow our plan, whether it is in-licensing or in-house research, we can build a sustainable oncology company. We can't affect the current market conditions, yet through our hard work and implementation, we plan to be in the oncology business for the long term.

OBR: *You've got a lot to get done this year.*

JB: We feel we've accomplished a lot, and we have a lot of ambitious goals for '08, but we also feel as though we're right where we want to be. Drug development is a risky business and while not everyone agrees with a multi-product pipeline, I continue to believe that "multiple shots on goal" is the appropriate business model to follow in building a viable drug development business and ultimately creating sustainable shareholder value.



EntreMed, Inc.

9640 Medical Center Drive, Rockville, Maryland 20850

240-864-2600 (p)

240-864-2601 (f)

www.entremed.com