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Presentation Overview

- Corporate Situational Breakdown
- Account of Intellectual Property Holdings
- Intellectual Property Utilization Analysis
- Recommendations

Corporate Situational Breakdown

- Corporate Profile / Goals
- Finances
- Competition
- Risk Factors
- Products

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Corporate Profile / Goals

- EntreMed, Inc. is a clinical-stage pharmaceutical company
 - Founded 1991, IPO 1996
 - Currently 38 employees
- Goals
 - Conduct research into angiogenesis; develop therapeutics for the treatments of inflammatory diseases and cancer
 - Commercialization
 - Strategic Partnerships
 - Licensing Arrangements

EntreMed, Inc. is a clinical-stage pharmaceutical company focused on developing next generation multi-mechanism oncology and anti-inflammatory drugs that target disease cells directly and the blood vessels that nourish them.

Angiogenesis is the physiological process involving the growth of new [blood vessels](#) from pre-existing vessels. Though there has been some debate over this, [vasculogenesis](#) is the term used for spontaneous blood-vessel formation, and [intussusception](#) is the term for new blood vessel formation by splitting of existing ones.

Angiogenesis is a normal process in growth and development, as well as in wound healing. However, this is also a fundamental step in the transition of [tumors](#) from a dormant state to a [malignant](#) state.

EntreMed's plan is to pursue many product candidates simultaneously. Corporate documents indicate the company's intention to aggressively pursue co-development alliances, funded research and licensing opportunities, as well as partnerships with pharmaceutical and biotechnology companies.

Finances

- IPO 1996
- FYR 2005
 - Revenue: 5.92M
 - Net Income: -16.3M
 - Total Assets: 36.43M (30.1M cash)
- Will increase research and development spending in 2006

Since December 2004, EntreMed raised nearly \$55 million through the sale of common stock to institutional investors and through the exercise of warrants held by Celgene Corporation. The company believes that the proceeds from these transactions, together with its cash, short-term investments and projected cash inflows, will support current and planned operations well into 2007.

EntreMed raised an additional 30M in gross proceeds through a private placement of common stock and warrants to institutional biotech investors

Competition

- Many existing and potential competitors have substantially greater financial, technical and human resources

Competition in the pharmaceutical, biotechnology and biopharmaceutical industries is intense and based significantly on

The availability of patent and other protection

The ability and length of time required to obtain governmental approval

Manufacturing & Marketing

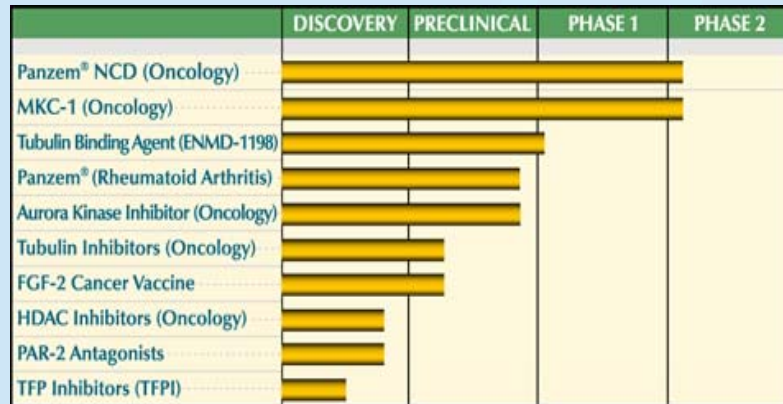
Ability to commercialize products in a timely fashion

Risk Factors

- **Development of Products is at an Early Stage and is Uncertain**
 - results of research and development activities
 - progress of preclinical studies or clinical trials
 - changes in or terminations of our relationships with strategic partners
 - competitive and technological advances
 - marketing and sales capabilities
 - manufacturing
 - the regulatory approval process

Products

Product Pipeline



Panzem, 2-methoxyestradiol or 2ME2, is EntreMed's lead clinical candidate. The 2ME2 mechanisms that are particularly relevant to the treatment of cancer involve inhibiting endothelial cell growth (antiangiogenic activity) and killing tumor cells directly (pro-apoptotic activity). Panzem was developed internally by EntreMed, and the Company owns exclusive rights to it.

MKC-1 is an orally-active, small molecule, cell cycle inhibitor with a unique mechanism of action. Specifically, MKC-1 arrests cellular mitosis by inhibiting a novel intracellular target important in cellular trafficking that has been shown to be involved in cell division. MKC-1 was acquired from in January 2006 when the company acquired Miikana Therapeutics, Inc., a clinical-stage biopharmaceutical company with research laboratories in Toronto, Canada.

Strategic Partners

- Research & Development Agreement with Bristol-Myers Squibb
- National Cancer Institute
- Research Agreements
 - Sponsored arrangements with outside scientists (e.g. University of Maryland) to conduct specific research projects

In 1995, EntreMed signed a Research Collaboration and License Agreement with Bristol-Myers Squibb Company which through fiscal year 1998, provided EntreMed with \$28.5 million. In 1999, EntreMed and Bristol-Myers Squibb jointly announced a modified Research and Development agreement allowing Entremed to re-assume development lead for the angiostatin protein.

One of EntreMed's strongest and most successful collaborations is with the National Cancer Institute. In September 1998, the National Cancer Institute, recognizing antiangiogenic cancer therapeutics as a promising strategy in the war on cancer, signed a Cooperative Research and Development Agreement (CRADA) with EntreMed to assist with clinical trials of Endostatin protein.

Account of Intellectual Property Holdings

- Registered Property
 - 19 patents
 - 3 trademarks

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Patents

Sub Areas

- Production Methods
- Methods for inhibiting cell proliferation
- Methods for treating angiogenic disease
- Other treatment methods

Angiostatin is a human protein. It is a natural angiogenesis inhibitor (i.e., it blocks the growth of new blood vessels), and it is currently underlying clinical trials for its use in anticancer therapy.

EntreMed's patent holdings can be classified into a few sub areas

Production Methods

6723536 Method of producing and purifying angiostatin
6090617 Flow electroporation chamber with electrodes having a crystalline metal nitride coating
6074605 Flow electroporation chamber and method
5720921 Flow electroporation chamber and method

Methods for inhibiting cell proliferation

6805865 Compositions and methods for treating cancer and hyperproliferative disorders
6734163 Compositions and methods for inhibiting cellular proliferation
5981471 Compositions and methods for inhibiting cellular proliferation
5919459 Compositions and methods for treating cancer and hyperproliferative disorders
5814666 Encapsulated and non-encapsulated nitric oxide generators used as antimicrobial agents
5605885 Method for Stimulating the Immune System

Methods for treating angiogenic disease

6593291 Compositions and methods of use of ligands that bind components of the blood coagulation/clotting pathway for the treatment of cancer and angiogenic-based disease
6544947 Compositions and methods for inhibiting endothelial cell proliferation and regulating angiogenesis using cancer markers
6518298 Methods and compositions for inhibition of angiogenesis with EM-138
6413513 Compositions and methods for inhibiting endothelial cell proliferation and regulating angiogenesis using cancer markers
6201104 Angiogenesis--inhibiting protein binding peptides and proteins and methods of use

Other treatment methods

6605622 Use of anti-estrogenic compounds as anti-fungal agents
6239123 Use of estrogenic compounds as anti-fungal agents
6224902 Vaccines against sterols
5753260 Vaccines against sterols

Trademarks

- “EntreMed”
- “The Angiogenesis Company”
- “Panzem”
- entremed.com (registered domain)

Intellectual Property Utilization Analysis

- IP Risk Factors
 - failure to obtain additional patents
 - challenge, invalidation, or circumvention of patents already issued
 - failure of the rights granted under patents to provide sufficient protection
 - independent development of similar products by third parties
 - ability of third parties to design around patents

IP Utilization

- EntreMed's Current Practice
 - Register patents for drugs and processes
 - Register TM names for drugs as they approach market readiness
 - TM various slogans

Patent Usage

- Active
 - Panzem
 - MKC-1
 - Others
- Inactive
 - 5 patents in areas outside the main focus of the company
 - anti-fungal medicines
 - sterol vaccines

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Active:

Panzem: Production methods for Angiostatin, methods for treating angiogenic disease

MKC-1: Methods for inhibiting cell proliferation

Others: Methods for treating angiogenic disease

Inactive:

EntreMed has 5 patents in areas outside the main focus of the company. The areas of the patents include anti-fungal compounds and vaccines against sterols. We can explore methods of earning revenue from this unused intellectual property. EntreMed can either license or sell the rights to their patents to companies that specialize in the anti-fungal medicines and vaccines against sterols. We also recommend that a search is performed to see if any companies are currently infringing the intellectual property rights of EntreMed and to pursue the appropriate legal actions against the infringers.

Sterols, or **steroid alcohols** are a subgroup of steroids. Sterols are important for the physiology of eukaryotic organisms. They form part of the cellular membrane where they modulate their fluidity and function and participate as secondary messengers in developmental signaling.

Different organisms utilize different sterols. The most important ones are cholesterol, phytosterols, and some steroid hormones in animals.

Trademark Usage

- “The Angiogenesis Company” no longer appears in company literature
- Since 1996 EntreMed has abandoned several trademarks

Selected abandoned trademarks

WE'RE NOT MAKING BETTER BLOOD, WE'RE MAKING BLOOD BETTER

DOING WELL BY DOING GOOD

PHOSAIC

ENTREVEST

VASCULOSTATIN

APOMIDE

...

Recommendations

- IP Protection Under Joint Ventures
- Partnerships for Manufacture and Marketing
- Reevaluation of Trademark Practices
- Licensing Unused IP
- Registering the EntreMed Logo
- Acquiring Additional Domains
- Angiogen

IP Protection Under Joint Ventures

Employees

- non-disclosure and non-compete agreements
- review of all the advanced laboratory and research techniques
- feasibility study for patenting such techniques

Sponsored Research Agreements

- secure the rights to develop under exclusive license any discoveries resulting from these collaborations

Example:

Elan Corporation, plc (NYSE: ELN) and EntreMed, Inc. (NASDAQ: ENMD) today announced that they have entered into a License Agreement in which EntreMed has been granted rights to utilize Elan's proprietary NanoCrystal Technology to develop the oncology product candidate, Panzem® NCD (2ME2 or 2-methoxyestradiol). Under the terms of the License Agreement, Elan is eligible to receive payments upon the achievement of certain clinical, manufacturing, and regulatory milestones. Additionally, Elan will receive royalty payments based on sales of Panzem® NCD. (Source: biotechindustryblog.com 1/10/06)

Partnerships for Manufacture and Marketing

- EntreMed has no large-scale manufacturing or marketing capacity
- Consider a partnership with a large pharmaceutical company now
 - Minimize time-to-market
 - Contracts should be drafted to protect EntreMed's production processes

Examples:

Bayer and Schering-Plough form partnership: Bayer said yesterday [September 14, 2004] that it had entered a partnership with Schering-Plough for marketing and distribution of Bayer's primary care pharmaceuticals, including the impotence drug Levitra in the United States and Puerto Rico. The deal will reduce Bayer's health care costs in the United States by 75 percent, affecting 1,800 jobs that will be cut or transferred to Schering-Plough, based in Kenilworth, N.J. Bayer, based in Leverkusen, Germany, will focus its United States health care business on profitable specialty drugs, biotechnology products and will start an oncology business unit with headquarters in West Haven, Conn. Petra Kappl (Source: New York Times Online Archive 9/14/04)

Partnership between Merck and Schering-Plough. Sales for Vytorin, a cholesterol-treating combination produced by Merck and Schering-Plough, have grown since its market debut last summer, but the drug's real test lies ahead, analysts say. Vytorin contains Zetia, a drug produced by Schering-Plough that inhibits absorption of cholesterol into the liver and intestine, and Zocor, the Merck blockbuster that cuts cholesterol. (Source: CNN Money 6/20/2005)

Reevaluation of Trademark Practices

- Get out of business of inventing and trade marking drug names
- Get out of Slogan Business
 - Most of this property ends up unused
 - Prospective partners will be much better equipped to handle this

Licensing Unused IP

- Consider licensing or selling sterol patents to companies that produce cholesterol lowering drugs.
- Anti-fungal patents could be licensed to any number of companies that manufacture anti-fungal medications.
- Funds could be used to increase research investments into the current pipeline.

Cholesterol:

Pfizer (Lipitor)

AstraZeneca Pharm. (Crestor)

Merck & Schering Plough Partnership (Vytorin)

Anti-fungal:

Pfizer (fluconazole, Eraxis)

Procter & Gamble (pyrithione zinc)

Registering the EntreMed logo


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-ENTREMED


Acquiring Additional Domains

- entremed.net
- panzem.com
- entermed.com

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- Possible patent infringement: Angiogen and EntreMed both have patents on Angiostatin production
- EntreMed owns the TM “The Angiogenesis Company”
- Defend, License, or Sell



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Angiogen’s patent #6576609; Methods & Compositions for Generating Angiostatin
EntreMed’s patent #6723536; Method of Producing and Purifying Angiostatin

Angiogen has one main patent #6576609 that covers methods and composition for generating angiostatin. This production method of angiostatin patented by Angiogen could infringe upon EntreMed’s patent #6723536. We would suggest a further investigation of the similarities between the processes because the end result product is angiostatin in both patents.

We noted earlier that the trademark “The Angiogenesis Company” has fallen into disuse. We recommend that EntreMed consider either attempting to defend this trademark against possible infringement by Angiogen (should the EntreMed marketing department wish to resurrect the mark) or otherwise consider selling this mark to the Angiogen rather than loose it at no benefit. This trademark of “The Angiogenesis Company” could come into play during negotiations with Angiogen about the possible patent infringement.

Then it could be decided whether to license, create a joint partnership, or pursue litigation against Angiogen with respect to patent infringement. EntreMed has been in the business of producing oncology drugs that target disease cells directly and was founded 4 years earlier. In addition, EntreMed is further along in clinical trials with the FDA for their angiogenesis drug Panzem than Angiogen who is a Phase I trial. Finally, since EntreMed is a publicly traded company and Angiogen is still a privately owned, there is much more transparency into EntreMed’s business and IP usage.

Final Remarks

- EntreMed is a small company totally dependant on intellectual property
- Only if it is able to successfully secure and commercialize it's IP, will EntreMed ever see profits

Questions

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if you build it, we will come

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