Forward-Looking Statements

Certain statements contained herein are not strictly historical and are "forward looking" statements as defined in the Private Securities Litigation Reform Act of 1995. These statements include, without limitation, statements with respect to the company’s clinical development programs and the timing of initiation and completion of its clinical trials. Forward-looking statements are statements that are not historical facts, and can be identified by, among other things, the use of forward-looking language, such as "believes," "feels," "expects," "may," "will," "projects," "should," "seeks," "plans," "schedule to," "anticipates" or "intends" or the negative of those terms, or other variations of those terms of comparable language, or by discussions of strategy or intentions. A number of important factors could cause actual results to differ materially from those projected or suggested in the forward looking statement, including the risk factors described in Point's quarterly report on Form 10-K for the year ended December 31, 2005 and from time to time in Point's periodic and other reports filed with the Securities and Exchange Commission.
Agenda

• Overview

• Dual Mechanism of Action in Cancer
  – Stromal Targeted Activity
  – Targeted Immunostimulatory Activity

• Summary

• Q&A
Speakers

• **Barry Jones, Ph.D.**, Chief Scientific Officer, Senior Vice President of Research
  Recently promoted to Chief Scientific Officer, Senior Vice President, Barry has served as Vice President of Research of Point since January 2000 and Director of Immunology at Point since 1997. Prior to joining Point, he was Director of Immunology at Procept, Inc. from 1993 through July 1997. Barry has also held academic research positions at Yale University’s School of Medicine and at Pennsylvania State University.

• **Charles A. Dinarello, M.D.**, Professor of Medicine, University of Colorado School of Medicine
  Dr. Dinarello is a Professor of Medicine at the University of Colorado School of Medicine, a member of the U.S. National Academy of Sciences and the author of over 500 published research articles. In addition to his active academic research career, Dr. Dinarello has held advisory positions with two branches of the National Institutes of Health and positions on the Board of Governors of both the Weizmann Institute and Ben Gurion University. Dr. Dinarello received his medical degree from Yale University and clinical training at the Massachusetts General Hospital.
Point Therapeutics Overview

• Novel therapeutics
  – Developing portfolio of dipeptidyl peptidase (DPP) inhibitors for use in cancer, type 2 diabetes and as vaccine adjuvants

• Lead product – talabostat (PT-100)
  – Oral agent
  – Potential as a broad anti-tumor agent
    • To treat solid tumors and blood cancers
  – Studied in more than 450 humans
## Point Therapeutics Oncology Program

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<thead>
<tr>
<th>TALABOSTAT</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<td><strong>NSCLC</strong> w/docetaxel</td>
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<td><strong>Metastatic Melanoma</strong> single-agent</td>
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<td><strong>CLL</strong> w/rituximab</td>
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<td><strong>Pancreatic Cancer</strong> w/gemcitabine</td>
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Talabostat – First DPP Inhibitor in Oncology

• First-in-class targeted agent with a novel dual mechanism of action unique in oncology
• Targeted Fibroblast Activation Protein (FAP) inhibition in tumor stroma
• Stimulation of innate and acquired immunity though targeted inhibition of two DPPs
• Today, talabostat’s targets and mechanism of action will be elucidated for the first time
Dual Mechanism of Action Overview
### Dipeptidyl Peptidases (DPPs) Overview

- **What are DPPs?**
  - Belong to the family of serine proteases
  - Enzymes found naturally in the body
  - Regulate biological processes, including tumor growth and immune responses
DPPs in Oncology

• There are five known active DPPs: 2, 4, 8, 9 and FAP

• In oncology, we believe there are three DPPs that are important to talabostat’s mechanism of action
The Role of Fibroblast Activation Protein (FAP)
Why is FAP an Important Target?

- Most normal tissues lack detectable FAP
- FAP expression induced in reactive stromal fibroblasts in >90% human epithelial carcinomas\(^1,2,3\)
  - Lung
  - Pancreatic
  - Colorectal
  - Ovarian
  - Breast
- FAP expressed in melanoma
- FAP expressed in some bone and soft tissue sarcomas\(^4\)

\(^{2}\)Huber, M.A. et al. J. Invest Dermatol. 120: 182-188
\(^{3}\)Dolznig, H. et al. Cancer Immunity 5: p.10
FAP Functions Based on Current Literature

Tumor Stromal Fibroblasts

FAP Breakdown of Extracellular Matrix

FAP Activation of Latent Growth Factors

Induction of FAP by Tumor

FAP-Mediated Intravasation into Circulation

Tumor Cells
FAP is Clearly Present as a Target in Human Embryonic Kidney (HEK293) Tumors Growing in Immunodeficient Mice

Promotion of HEK293 Tumor Growth by FAP Requires Enzymatic Activity

Day 21: xenograft DPP activity

Tumor growth

Preclinical Studies Indicate Tumor-Targeted FAP Inhibition

Talabostat Inhibits FAP Enzymatic Activity Thereby Suppressing Tumor Growth
Inhibitors of FAP Suppress Tumor Growth of HEK-FAP Xenografts in Immunodeficient Mice

- PT-630 was used to inhibit FAP independently of immune stimulation.

The Role of Fibroblast Activation Protein (FAP)

Promotion of Growth and Increased Microvessel Density by FAP in Human Breast Adenocarcinoma Xenografts in Immunodeficient Mice

Huang, Y., Wang, S. and Kelly, T. Cancer Res. 64: 2712-2716, 2004
Conclusions Based on Preclinical Data

• FAP is a validated tumor target
• FAP promotes tumor growth
• FAP is expressed in >90% of solid tumors
• FAP is a direct target for talabostat
• Inhibition of FAP can result in anti-tumor activity
Targeted Immunostimulatory Activity
Talabostat Inhibits DPP 8/9 Within the Macrophage
DPP 8 and DPP 9

- Close DPP relatives
- Expressed in the same cytoplasmic location
- Identical enzymatic activity
- Example of biologic redundancy
### Talabostat IC$_{50}$ Values

<table>
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<th>DPP</th>
<th>IC$_{50}$</th>
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<tr>
<td>FAP</td>
<td>32nM</td>
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<tr>
<td>DPP 8</td>
<td>3nM</td>
</tr>
<tr>
<td>DPP 9</td>
<td>3nM</td>
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</table>
Talabostat’s Inhibition of DPP 8/9 Causes Caspase-1 Activation
Caspase-1 Activation Causes Maturation and Secretion of IL-1β
DPP 8/9 Inhibition Activates Caspase-1 Causing IL-1β Secretion

• PTX-1200 and PTX-1210 are DPP 8/9 specific inhibitors
**IL-1β Stimulates Production of Cytokines and Chemokines**

- **Macrophage**
  - Conditioning Factor
  - Cytokines & Chemokines
  - DPP 8/9
  - Caspase-1
  - IL-1β
  - Autocrine loop

- **Fibroblast**
  - Cytokines & Chemokines
  - IL-1R
  - Paracrine loop

- **Talabostat PT-100**

The diagram illustrates the interaction between IL-1β and its effects on cytokine and chemokine production in both macrophages and fibroblasts.
Talabostat Initiates Cytokine/Chemokine Responses in Monocytes via IL-1β

**IL-1α**

- PT-100
- PT-100/anti-IL-1β

**IL-6**

- PT-100
- PT-100/anti-IL-1β

**G-CSF**

- PT-100
- PT-100/anti-IL-1β

**CXCL1/GROα**

- PT-100
- PT-100/anti-IL-1β
Talabostat Stimulation of Cytokine and Chemokine Expression in Tumor-Bearing Mice

Adams S. et al. Cancer Res. 64: 5471-5480, 2004
Preclinical Studies Demonstrate Talabostat’s Targeted Immunostimulation

Talabostat

Macrophage (DPP 8/9)
Stromal Fibroblasts

IL-1β

Inhibition of DPP 8/9 by Talabostat Induces an IL-1β Response (via Caspase-1) in the Stroma of Tumor & Lymph Nodes

Cytokines & Chemokines

INNATE IMMUNITY

Neutrophils
Macrophages
Natural Killer Cells

ACQUIRED IMMUNITY

Cytolytic T-Lymphocytes
Memory Cells

Chemokines

Tumor

Chemokines
Talabostat Monotherapy Preclinical Studies

- T-cell dependent anti-tumor effect (syngeneic mouse models)
  - 50-70% tumor rejection
  - Priming of CTL responses
  - Immunity to rechallenge

- T-cell independent anti-tumor effect (human tumor xenograft models)
  - 50->90% inhibition of tumor growth
  - Innate response (neutrophils)
Talabostat Suppression of B16 Melanoma Growth Requires IL-1 Receptor Signaling

B6 wild type mouse

- Saline
- PT-100 (10 µg)
- PT-100 (40 µg)

B6 IL-1 receptor knockout mouse

Tumor volume (c.c.)

Days

P<0.005
• Charles A. Dinarello, M.D., Professor of Medicine, University of Colorado School of Medicine
Properties of IL-1β and Talabostat

What do we know about these properties of IL-1β?

• In vitro, IL-1β induces chemokines and endothelial adhesion molecules
• In vivo, IL-1β causes the release of neutrophils from the bone marrow in mice and humans

What do we know about this property of talabostat?

• In mice, talabostat increases neutrophils in the blood and tumors
• In humans, talabostat increases neutrophils in the blood
Injection of IL-1β into Humans Increase Blood Neutrophil Counts

Day 20 Neutrophil Infiltration of Lung Carcinoma A549 Xenografts
What Else Contributes to the Immunostimulatory Property of IL-1\(\beta\)?

- In addition to IL-1\(\beta\) induction of chemokines there is also an induction of IL-1\(\alpha\).

- What is the function of IL-1\(\alpha\)?
  - In mice, IL-1\(\alpha\) functions to enhance the immunological response to tumors as well as the immunological mediated killing of tumors. This is a function of cell-membrane IL-1\(\alpha\).
IL-1β Upregulation of IL-1α Contributes to the Immunostimulatory Properties of Talabostat
Immunostimulatory Effects of IL-1α

A

Lysis of target cells (%)
40
30
20
10
0

Effector-to-target cell ratio
50:1 100:1 200:1

NK

CT, WT, MK
pIL-1α

mIL-1β
ssIL-1β

B

Lysis of target cells (%)
40
30
20
10
0

Effector-to-target cell ratio
5:1 10:1 20:1

CTL

pIL-1α

WT, MK
mIL-1β
ssIL-1β

Targeted Immunostimulatory Activity
Anti-Tumor Effect of Talabostat Against Established EL4 Lymphoma

Day 20

Tumor volume (cm$^3$)

- Saline
- PT-100 (20 µg)

$P < 0.00005$
Specific Immunity Following EL4 Lymphoma Regression in Mice Treated with Talabostat

![Graph showing tumor volume changes over time for EL4 and unrelated tumors in naive, rechallenge, B16, and Lewis lung conditions.](image-url)
IL-1 as Part of Talabostat’s Dual Mechanism of Action

• Talabostat is the only known anti-tumor agent requiring a functional IL-1 receptor for anti-tumor activity in mice—a unique finding.
• Immunostimulatory effects of IL-1\(\beta\) consistent with established activities:
  — Mobilization of neutrophils
  — Influx of neutrophils to sites of local inflammation such as tumors
• Together with inhibition of FAP by talabostat, local infiltration of neutrophils, macrophages and natural killer cells contribute to anti-tumor activity
• Ability of IL-1\(\beta\) to induce IL-1\(\alpha\) in tumors may increase immunological response to tumors as well as the immunological mediated killing of tumors
Preclinical studies indicate that the inhibition of DPP 8/9 induces an IL-1\(\beta\) response stimulating the production of cytokines and chemokines which in turn promote both innate and acquired immune responses against the tumor.
Talabostat’s Preclinical Proof of Concept in Support of Clinical Program
### Talabostat Proof-of-Concept

#### Preclinical
- 25+ tumor models in mice
- Significant response demonstrated with chemotherapy
  - Docetaxel
  - Pemetrexed
  - Dacarbazine
  - 5-FU
- Significant response demonstrated with monoclonal antibodies and targeted therapies
  - Rituximab
  - Trastuzumab
- Proof-of-concept as a single-agent

#### Clinical
- Demonstrated activity in advanced NSCLC, melanoma, NHL and CLL
- Demonstrated activity with chemotherapy
  - Docetaxel
  - Cisplatin
  - Gemcitabine
  - Paclitaxel
- Demonstrated activity with monoclonal antibody
  - Rituximab
  - Erlotinib
  - Bevacizumab
- Proof-of-concept as a single-agent in melanoma
Investigation of Anti-Tumor Effect of Docetaxel + Talabostat in A549 NSCLC Xenograft Model

<table>
<thead>
<tr>
<th>Day</th>
<th>Docetaxel</th>
<th>14D X PT-100</th>
<th>7D X Rest</th>
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<tbody>
<tr>
<td>D7</td>
<td>D8-21</td>
<td>D22-28</td>
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<td>D29</td>
<td>D30-43</td>
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<tr>
<td>D51</td>
<td>D52-65</td>
<td>D66-72</td>
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</table>
Anti-tumor Effect of 3 Cycles of Docetaxel and Talabostat in A549 NSCLC Xenograft Model

Day 20 Neutrophil Infiltration of Lung Carcinoma A549 Xenografts

Saline

Talabostat
Summary
Preclinical Studies Support Talabostat’s Dual Mechanism of Action

Preclinical Studies Indicate Tumor-Targeted FAP Inhibition

Talabostat Inhibits FAP Enzymatic Activity
Thereby Suppressing Tumor Growth

Preclinical Studies Demonstrate Talabostat’s Targeted Immunostimulation

Inhibition of DPP 8/9 by Talabostat Induces an IL-1β Response (via Caspase-1) in the Stroma of Tumor & Lymph Nodes

Cytokines & Chemokines

FAP Breakdown of Extracellular Matrix

FAP Activity of Latent Growth Factors

Tumor Stromal Fibroblasts

Talabostat

Tumor

FAP-Mediated Intravasation into Circulation

Macrophage

DPP 8/9

Stromal Fibroblasts

INNATE IMMUNITY

ACQUIRED IMMUNITY

Neutrophils

Macrophages

Natural Killer Cells

Cytolytic T-Lymphocytes

Memory Cells

Chemokines

Chemokines

Tumor
• Talabostat’s dual mechanism of action introduces a novel approach to the treatment of cancer because it combines both tumor-targeted and immunostimulatory activity in a single oral agent.

• Preclinical studies suggest that talabostat is an oral DPP inhibitor with anti-tumor activity achieved by targeting tumor stromal FAP and macrophage-associated DPP 8 and DPP 9. Inhibition of FAP can suppress tumor growth, and inhibition of DPP 8 and 9 can stimulate innate and adaptive immune responses that kill tumor cells.
## Projected Talabostat Development Timeline

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<tr>
<th>Disease</th>
<th>2004</th>
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<td>Phase 2 POC (w/ docetaxel)</td>
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<tr>
<td>Phase 3 Program</td>
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*Assuming adequate financial resources
Upcoming Talabostat Presentations

• Clinical
  – CLL Phase 2 Results Second Half 2006
  – Pancreatic Cancer Phase 2
    • Interim Results Second Half 2006
    • Final Q4 ‘06/Q1 ‘07

• Scientific Presentations
  – ASCO Q2
  – ASH Q4

• Quarterly Call – May 9, 2006
Summary

• First DPP inhibitor in oncology
• Talabostat has a novel dual mechanism of action with identified targets
  – Stromal targeted activity via FAP inhibition
  – Targeted immunostimulatory activity via DPP 8/9 inhibition
• Clinical studies demonstrate biological activity as a single-agent and in combination with standard chemotherapies and targeted therapies
• Multiple Phase 2 trials and investigator-sponsored trials ongoing
• Two Phase 3 studies in metastatic NSCLC are enrolling
Question and Answer