SBIR Phase IIB Bridge Award

Presented to
National Cancer Advisory Board

Presented by
Andrew J. Kurtz, PhD

September 13, 2011
PHASE I – R41, R43
• Feasibility Study
• $150K and 6-month (SBIR) *
• or 12-month (STTR) Award

PHASE II – R42, R44
• Full Research/R&D
• $1M and 2-year Award (SBIR & STTR) *
• Commercialization plan required

PHASE III
• Commercialization Stage
• Use of non-SBIR/STTR Funds

* Note: Actual funding levels may differ by topic.
Competing Renewal Program for SBIR Phase II Awards

- Provides additional NIH funding to extend selected projects
- Involves another peer-review cycle to evaluate progress & future plans
- Accelerates commercialization by incentivizing partnerships with third-party investors & strategic partners earlier in the development process

How do we accomplish this goal?

- NCI gives competitive preference and funding priority to applicants that can raise substantial third-party funds (i.e., ≥ 1:1 match)

“…Applicants are expected to leverage their previous NIH SBIR support, as well as the opportunity to compete for additional NCI funding under this [funding announcement], to negotiate and attract third-party financing needed to advance a product or technology toward commercialization…”
What does the NCI get?

• Opportunity to leverage millions of dollars in external resources
• Valuable input from third-party investors:
  1. Rigorous commercialization due diligence prior to award
  2. Commercialization guidance during the award
  3. Additional financing beyond the Bridge Award project period

What do the third-party investors get?

• Opportunity to partner with small businesses to develop & commercialize:
  1. Technologies that have been vetted by the NIH peer-review process, **AND**
  2. Projects for which a substantial amount of proof-of-concept data already exists

➢ **Opportunity to share in the early-stage investment risk with the NCI**
EXAMPLE: Drug Development

Target Identification & Validation

Preclinical Development (Lead Development, Animal Studies, File IND)

Safety Review (IND)

Clinical Trials

NDA Review

Commercialization

Phase I & Phase II SBIR

Private Investment / Strategic Partner

The “Valley of Death” is the problem
EXAMPLE: Drug Development

SBIR Bridge Award is designed to bridge the “Valley of Death”

Up to $1 M per year for 3 years ($3 M total) from the NCI
EXAMPLE: Drug Development

Target Identification & Validation
Preclinical Development (Lead Development, Animal Studies, File IND)
Safety Review (IND)
Clinical Trials
NDA Review
Commercialization

Phase I & Phase II SBIR
SBIR Bridge Award
Private Investment / Strategic Partner

Competitive applicants for the SBIR Bridge Award are expected to secure additional funding from Third-Party Investors to share in the investment risk.
Technical Scope

Cancer Therapeutics (FY09)
- Small molecule anticancer agents
- Anticancer biologics, including therapeutic vaccines
- Multifunctional cancer therapeutics based on nanotechnology
- Anticancer drug delivery systems

Cancer Imaging Technologies, Interventional Devices & In Vivo Diagnostics (FY09)
- Medical devices for in vivo cancer imaging and image-guided interventions
- Radiation therapy devices and other ablative techniques
- Imaging agents, including imaging radiopharmaceuticals
- Devices and technologies for in vivo cancer diagnostics

In Vitro and Ex Vivo Cancer Diagnostics and Prognostics (New in FY10)
- Molecular diagnostics and prognostics, including in vitro diagnostic multivariate index assays (IVDMIA)
- Image analysis tools for diagnosis
- Spectroscopic techniques for in vivo and ex vivo tissue analysis

Opportunity to impact >75% of the Phase II projects in NCI’s SBIR portfolio
Eligibility

- Current Phase II awards & and those that ended within the last 2 years
- Cancer-related Phase II projects initially funded by other NIH institutes

Special Review to Evaluate Technical and Commercial Merits

- Reviewers are academics, clinicians, industry professionals, venture capitalists
- Emphasizes important commercialization considerations such as intellectual property (e.g., patents) and strategy for gaining FDA approval
- Requires complete disclosure of applicant’s SBIR commercialization history

➢ Third-Party Fundraising plan

- **Preferred Types of Funds:** Cash, liquid assets, convertible debt
- **Sources of Funds:** Another company, venture capital firm, individual “angel” investor, foundation, university, state or local government, or any combination
How are we sure that they need more money from the NCI?

Applicants must provide a concise “Statement of Need” that includes answers to the following questions:

• What is the perceived “Valley of Death” for the product/technology?

• Why is additional government funding critically needed to accelerate the development of the product or technology toward commercialization?

• What activities are being proposed that would not otherwise be possible through independent third-party investments OR would be significantly delayed without additional NIH support?

• To what extent would a possible award advance the product or technology far enough to attract sufficient, independent third-party financing and/or strategic partnerships to carry out full commercialization?
71 unique applications received to date (17 were resubmitted)
10 projects funded to date

Overall success rate: 14%

<table>
<thead>
<tr>
<th>RFA #</th>
<th>FY</th>
<th>Date</th>
<th>Therapeutics</th>
<th>Imaging</th>
<th>Diagnostics/Prognostics</th>
<th>Total</th>
<th>Funded</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA08-021</td>
<td>2009</td>
<td>Sep 2008</td>
<td>11</td>
<td>12</td>
<td>0</td>
<td>24</td>
<td>2</td>
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<td></td>
<td></td>
<td>Feb 2009</td>
<td>9</td>
<td>10</td>
<td>0</td>
<td>19</td>
<td>4</td>
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<tr>
<td>CA10-009</td>
<td>2010</td>
<td>Mar 2010</td>
<td>8</td>
<td>10</td>
<td>8</td>
<td>26</td>
<td>4</td>
</tr>
<tr>
<td>CA11-002</td>
<td>2011</td>
<td>Apr 2011</td>
<td>5</td>
<td>7</td>
<td>7</td>
<td>19</td>
<td>2*</td>
</tr>
</tbody>
</table>

* Pending Award
<table>
<thead>
<tr>
<th>FY</th>
<th>Company</th>
<th>Technology/Product</th>
<th>Award Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Lpath Therapeutics</td>
<td>Humanized monoclonal antibody for treatment of prostate cancer</td>
<td>$3,000,000</td>
</tr>
<tr>
<td>2009</td>
<td>Optosonics</td>
<td>Photoacoustic CT for preclinical molecular imaging</td>
<td>$2,997,247</td>
</tr>
<tr>
<td>2009</td>
<td>Guided Therapeutics</td>
<td>Fluorescence/reflectance spectroscopy for detection of cervical cancer</td>
<td>$2,517,125</td>
</tr>
<tr>
<td>2009</td>
<td>Koning Corporation</td>
<td>High-performance breast CT as diagnostic adjunct to mammography</td>
<td>$2,986,453</td>
</tr>
<tr>
<td>2009</td>
<td>Gamma Medica-Ideas</td>
<td>Molecular imaging to detect metabolic activity of breast lesions</td>
<td>$3,000,000</td>
</tr>
<tr>
<td>2010</td>
<td>20/20 GeneSystems</td>
<td>mTOR companion diagnostic assay</td>
<td>$2,750,000</td>
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<tr>
<td>2010</td>
<td>Advanced Cell Diagnostics</td>
<td><em>In situ</em> RNA detection assay for analyzing circulating tumor cells</td>
<td>$2,996,450</td>
</tr>
<tr>
<td>2010</td>
<td>Ambergen</td>
<td>Expression-based prognostic assay for recurrence of colorectal cancer</td>
<td>$2,998,830</td>
</tr>
<tr>
<td>2010</td>
<td>Praevium Research</td>
<td>High-performance imaging engine for optical coherence tomography</td>
<td>$1,180,420</td>
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</tbody>
</table>

Arrows:
- 2 therapeutics
- 5 imaging technologies
- 3 diagnostics

Summary:

- **NCI Total**: $27,395,816
- **Third-Party Investments**: $62,950,000
- **Leverage**: > 2 to 1
Ten Bridge Awards: FY09 – FY10

Venture Capital: ~1/3
Strategic Partners: ~1/3
Individuals & Other: ~1/3
Diseased cell or tissue

Intracellular tumor or viral protein

Proteolytic processing

Peptide antigen presentation in MHC complex

STAR™ molecules

STAR™ molecules target disease-specific antigens

Major histocompatibility complex (MHC)

T-cell receptor (TCR)

Drug ≡ IL-2 (ALT-801)

Tumor Cell Lysis
SBIR Phase I & Phase II

- ALT-801 inhibits growth or causes regression of human-derived cancer cells when grown in animal models
- ALT-801 shows significantly better antitumor activity than IL-2 alone
- ALT-801 was advanced as a clinical candidate and evaluated in a Phase I clinical study (ClinicalTrials.gov: NCT01029873)
  - Treated 26 patients with progressive metastatic p53-positive malignancies
  - Primary endpoints: Safety, maximum tolerated dose (MTD), pharmacokinetics
  - Secondary endpoints: Immunogenicity and antitumor response

➤ ALT-801 exhibited favorable safety and PK profiles at the MTD level
$3.0 million Phase II Bridge Award

- Further assessment of the anti-tumor activities of ALT-801 for advanced/metastatic melanoma, renal cell carcinoma, head and neck adenocarcinoma, and prostate cancer
- New therapeutic regimen has been developed for a clinical study in patients with metastatic melanoma

(ClinicalTrials.gov: NCT01029873)

- Eight clinical sites in the U.S. have been initiated and are screening patients for enrollment in this study
- Results of the dose escalation phase will be used to establish ALT-801 plus cisplatin treatment regimens in Phase II clinical studies for other indications

Third-Party Investment: $8,000,000

- In July 2008, Altor signed a term sheet to raise a total of $8.0M in a financing round led by Sanderling Ventures
- Bridge fundraising is complete, and additional funds have been raised beyond the original commitment
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Milestone-Based Awards

Ability to raise matching funds is a component of the Phase II Bridge Award

Phase II Award
- Year 1+

Milestones reached?
- Matching funds secured for year 1?

SBIR Bridge Award
- 1st Year
  - Portion of funds
  - YES
- 2nd Year
  - Portion of funds
  - YES
- 3rd Year
  - Portion of funds
  - YES

Milestones reached?
- Matching funds secured for year 2?

NO

Milestones reached?
- Matching funds secured for year 3?

NO

STOP

Private investor(s) / strategic partner(s) continue to support commercialization