SBIR Phase IIB Bridge Award

*RFA Concept Review (Reissuance)*

Presented to
NCI Board of Scientific Advisors

Presented by
Andrew J. Kurtz, PhD

June 20, 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 promising projects
• Helps selected projects/companies cross the “Valley of Death” by:
  • Incentivizing partnerships with third-party investors & strategic partners
  • Facilitating third-party investments earlier in the development process

How do we accomplish these goals?

• Program gives competitive preference and funding priority to applicants that can raise substantial third-party funds (i.e., ≥ 1:1 match)
  • Affords NIH the opportunity to leverage millions in external resources
  • Provides valuable input from third-party investors in several ways:
    1. Rigorous commercialization due diligence prior to award
    2. Commercialization guidance during the award
    3. Additional financing beyond the Bridge Award project period
Technical Scope: Cancer Therapies & Imaging Technologies

- Original concept developed in collaboration with staff from NCI’s Division of Cancer Treatment and Diagnosis (DCTD)
- Focus on areas requiring substantial capital for clinical validation & FDA approval
- Opportunity to impact >50% of the Phase II projects in NCI’s SBIR portfolio

Mechanism & Budgets

- Uses the SBIR Phase II (R44) competing renewal mechanism
  - Provides up to $1 M per year for up to 3 years ($3 M total)

Eligibility

- Current Phase II awards & and those ending within the last 2 years
- Cancer-related Phase II projects funded by other NIH institutes
  (must conform to the technical scope specified in the RFA)
Special Review Criteria

- Balanced consideration of technical and commercial merits
- Emphasis on IP and regulatory strategy
- Complete disclosure of applicant's SBIR commercialization history
- Fundraising plan*

Preferred 3rd-party Matching 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

* Applications with strong fundraising plans are rewarded with higher scores
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
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

The “Valley of Death” is the problem

SBIR Bridge Award addresses the problem by bridging the “Valley of Death”
EXAMPLE: Drug Development

SBIR Bridge Award allows NCI to share investment risk by incentivizing Private Investors to evaluate projects and commit funds much earlier.
Applicants must provide a concise “Statement of Need”. This statement is expected to provide answers to the questions listed below:

• 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?
### Applications Received

<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>
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<tr>
<td>CA08-021</td>
<td>2009</td>
<td>Sep 2008</td>
<td>11</td>
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<td>0</td>
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<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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<td>CA10-009</td>
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<td>Mar 2010</td>
<td>8</td>
<td>10</td>
<td>8</td>
<td>26</td>
<td>4</td>
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<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>Pending review</td>
</tr>
</tbody>
</table>

Program recommends reissuing the RFA each year for the next three years, with two receipt dates per year.
Ten Bridge Awards: FY09/FY10

San Diego, CA
$3.0M for the commercialization of ASONEP™, a first-in-class monoclonal antibody against the angiogenic growth factor S1P

Oriental, NC
$3.0M for the development of a photoacoustic computed tomography (CT) scanner for preclinical molecular imaging

Norcross, GA
$2.5M for the development of LightTouch®, a point-of-care device for cervical cancer screening

Northridge, CA
$3.0M for the development of a novel molecular breast imaging technique to guide early-stage patient care

Miramar, FL
$3.0M for the development of ALT-801, a fusion protein consisting of IL-2 coupled with a soluble T-cell receptor fragment that recognizes a specific form of processed p53 antigen

West Henrietta, NY
$3.0M for the development of a cone beam breast CT scanner
## Ten Bridge Awards: FY09/FY10

<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>
</tr>
<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>Amберgen</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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</table>

Total $27,395,816

- 2 therapeutics
- 5 imaging technologies
- 3 diagnostics
## Third-Party Investment

*Cumulative for Ten Bridge Awards (FY09/FY10)*

<table>
<thead>
<tr>
<th>Investor</th>
<th>Amount</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Traditional VC</td>
<td>$21,500,000</td>
<td>34%</td>
</tr>
<tr>
<td>Strategic Partners</td>
<td>$24,200,000</td>
<td>38%</td>
</tr>
<tr>
<td>Other Investment Firms</td>
<td>$5,500,000</td>
<td>9%</td>
</tr>
<tr>
<td>Individuals &amp; Others</td>
<td>$11,750,000</td>
<td>19%</td>
</tr>
</tbody>
</table>

**Investor Total**: $62,950,000  
**NCI Total**: $27,395,816  
**Leverage**: > 2 to 1
Milestone-Based Awards

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

Phase II Award

<table>
<thead>
<tr>
<th>Year 1+</th>
<th>Milestones reached?</th>
<th>Matching funds secured for year 1?</th>
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<td>STOP</td>
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SBIR Bridge Award

<table>
<thead>
<tr>
<th>1st Year</th>
<th>Portion of funds</th>
<th>Milestones reached?</th>
<th>Matching funds secured for year 2?</th>
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<tr>
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</table>

<table>
<thead>
<tr>
<th>2nd Year</th>
<th>Portion of funds</th>
<th>Milestones reached?</th>
<th>Matching funds secured for year 3?</th>
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</thead>
<tbody>
<tr>
<td>YES</td>
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<td>STOP</td>
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</table>

<table>
<thead>
<tr>
<th>3rd Year</th>
<th>Portion of funds</th>
<th>Milestones reached?</th>
<th>Matching funds secured for year 3?</th>
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</thead>
<tbody>
<tr>
<td>YES</td>
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</tbody>
</table>

Private investor(s) / strategic partner(s) continue to support commercialization.
Bridge Award (Pilot Phase)

NCI SBIR set-aside
- FY09: $5,999,861
- FY10: $5,984,792
- FY11: ~$5,485,463

Bridge funding
- FY09: $6.0 M
- FY10: $9.1 M
- FY11: ~$14 M

% of total SBIR
- FY09: 6.2 % (actuals)
- FY10: 9.2 % (actuals)
- FY11: ~14 % (estimated)

FY09 awards
- FY09: $5,999,861

FY10 awards
- FY10: $5,984,792

FY11 awards
- FY11: ~$5,485,463

FY11 awards (estimated): ~$5,000,000

FY10 awards (actuals): $3,394,381

FY09 awards (actuals): $3,147,361
Major histocompatibility complex (MHC)
T-cell receptor (TCR)

STAR™ molecules target disease-specific antigens

Drug ≡ IL-2
(ALT-801)
SBIR Phase I & Phase II

- Inhibits growth or causes regression of primary tumors derived from human p53-positive/HLA-A2.1 cancer cells in several xenograft models
- Exhibits significantly better antitumor activity than recombinant human IL-2 alone
- ALT-801 was advanced as a clinical candidate and evaluated in a Phase I clinical study (ClinicalTrials.gov: NCT01029873)
  - Treatment of 26 patients with progressive metastatic p53-positive malignancies
  - Primary endpoints: Safety, 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
- Cisplatin regimen has been developed to replace the ALT-801 monotherapy regimen for a Phase Ib/II 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
Enlight Biosciences Structure

- Guide Enlight focus areas
- Create “wish list”
- Invest in portfolio companies

Enlight Biosciences

- Endra
- Newco 2
- Etc.

NCI: $3M

Endra: $3M

OptoSonics

Johnson & Johnson

Abbott

Lilly

Merck

Novartis

Pfizer

PureTech Ventures
**Goal:** Develop a 3-D optical imaging technique with increased depth and resolution relative to current optical techniques

**How it works:** acoustic waves are generated when short pulses of light are absorbed by tissue

**Nexus 128:** uses a tunable laser and 128 acoustic receivers to produce multi-spectral images, in less than 1 minute
SBIR Phase IIB Bridge Award

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June 20, 2011
## Program Evaluation, Looking Ahead

### Summary
Applications Received Feb 2009

<table>
<thead>
<tr>
<th>Peer Review Rank</th>
<th>Score</th>
<th>Grant Number</th>
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Long-term, how do the outcomes for funded Bridge Award projects/companies compare to those that missed the cut?