

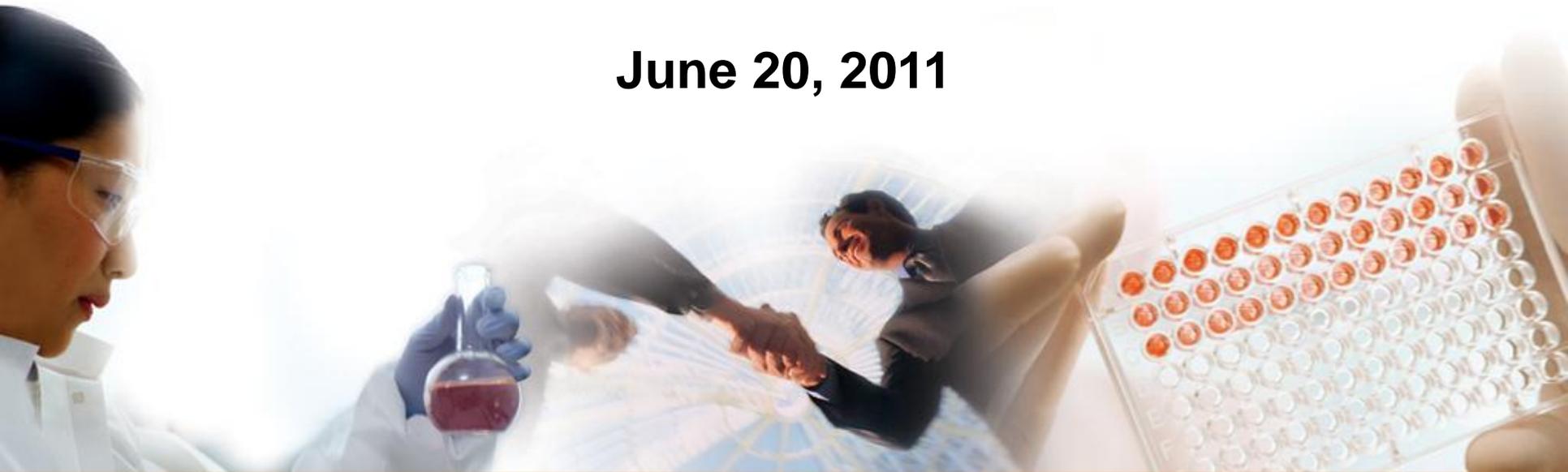
SBIR Phase IIB Bridge Award

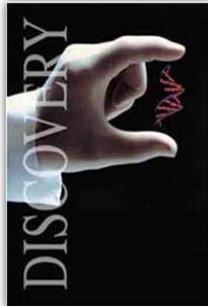
RFA Concept Review (Reissuance)

Presented to
NCI Board of Scientific Advisors

Presented by
Andrew J. Kurtz, PhD

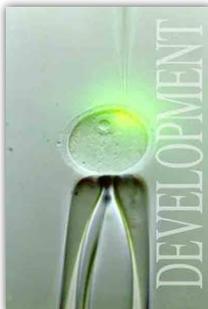
June 20, 2011





PHASE I – R41, R43

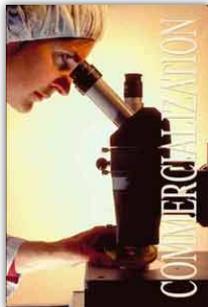
- Feasibility Study
- \$150K and 6-month (SBIR) *
- or 12-month (STTR) Award



PHASE II – R42, R44

- Full Research/R&D
- \$1M and 2-year Award (SBIR & STTR) *
- Commercialization plan required

Phase IIB Bridge Award



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., \geq 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***

Part I Overview Information

Department of Health and Human Services

Participating Organizations

National Institutes of Health (NIH), (<http://www.nih.gov>)

Components of Participating Organizations

National Cancer Institute (NCI), (<http://www.cancer.gov>)

Title: SBIR Phase II Bridge Awards to Accelerate the Development of New Cancer Therapies and Cancer Imaging Technologies Toward Commercialization (SBIR [R44])

Announcement Type

New

Request For Applications (RFA) Number: RFA-CA-08-021

NOTICE: Applications submitted in response to this Funding Opportunity Announcement (FOA) for Federal assistance must be submitted electronically through Grants.gov (<http://www.grants.gov>) using the SF424 Research and Related (R&R) forms and the SF424 (R&R) Application Guide.

APPLICATIONS MAY NOT BE SUBMITTED IN PAPER FORMAT.

This FOA must be read in conjunction with the application guidelines included with this announcement in [Grants.gov/Apply for Grants](http://Grants.gov/ApplyforGrants) (hereafter called Grants.gov/Apply).

A registration process is necessary before submission and applicants are highly encouraged to start the process at least four (4) weeks prior to the grant submission date. See [Section IV](#).

Apply for Grant Electronically

For Assistance downloading this or any Grants.gov application package, please contact Grants.gov Customer Support at <http://grants.gov/CustomerSupport>

Catalog of Federal Domestic Assistance Number(s)

93.394, 93.395

Key Dates

Release/Posted Date: May 14, 2008

Cancer Therapeutics (FY09)

- Small molecule anticancer agents
- Anticancer biologics, including therapeutic vaccines
- Multifunctional cancer therapeutics using nanotechnology
- Anticancer drug delivery

Cancer Imaging Technology

- Medical devices for image-guided interventions
- Radiation therapy optimization techniques
- Imaging agents, including contrast agents
- Devices and techniques for diagnostics

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

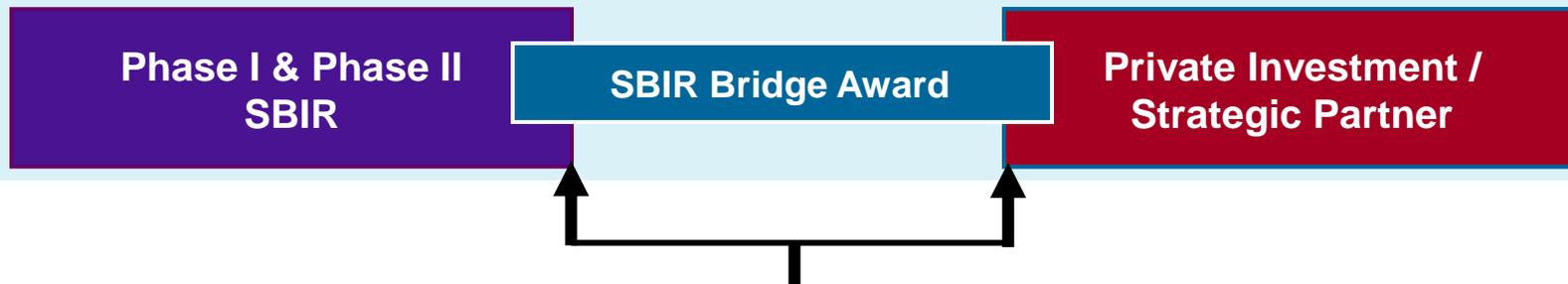
Image-guided Interventions & *In Vivo* Diagnostics (FY09)

- Image-guided interventions
- Techniques
- Contrast agents
- 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

EXAMPLE: Drug Development



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:

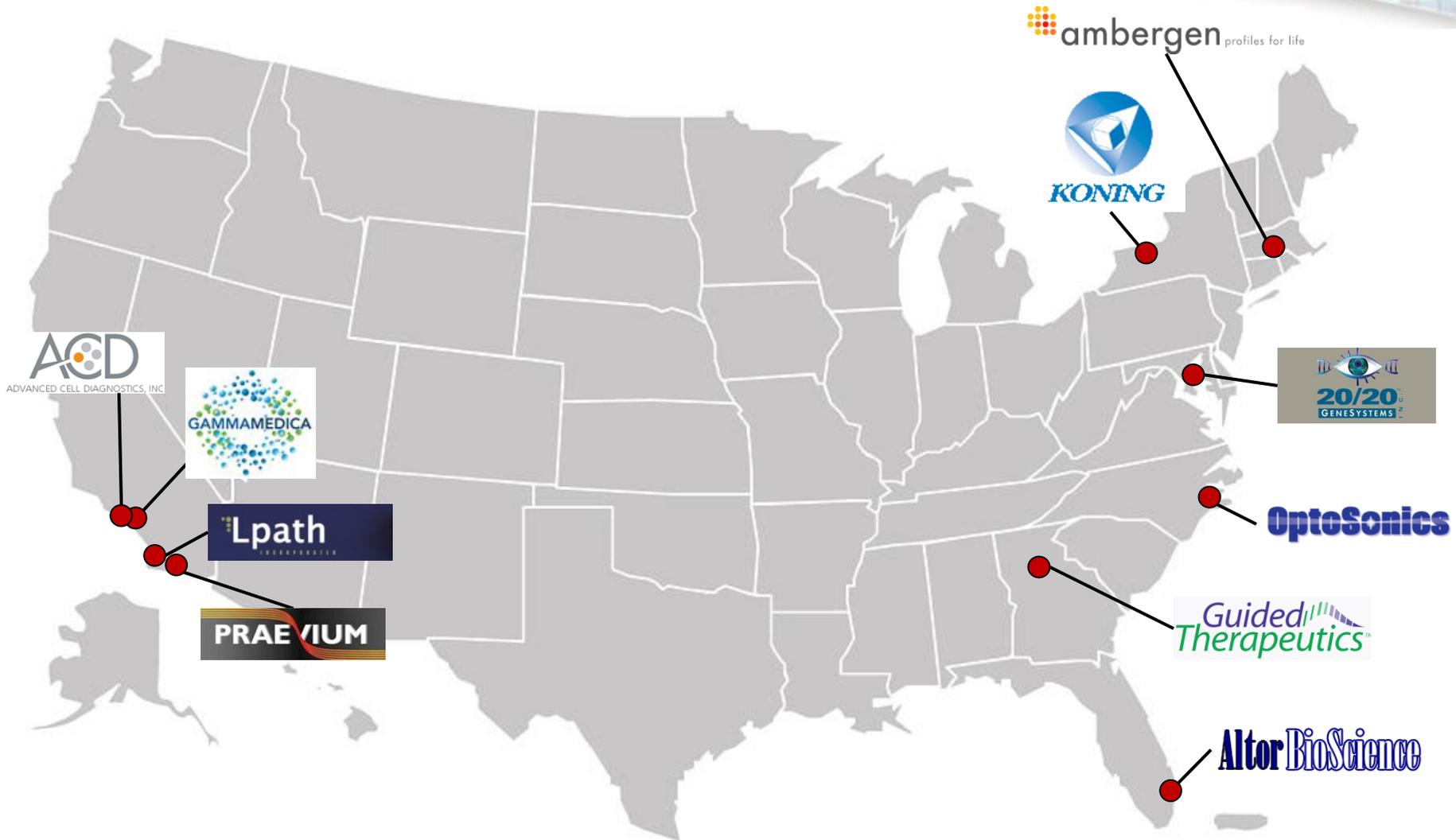
- What is the perceived “Valley of Death” for the product/technology?
- Why is additional government funding critically needed to accelerate the development of the product or technology toward commercialization?
- What activities are being proposed that would not otherwise be possible through independent 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 by Receipt Date

		Applications Received					
RFA #	FY	Date	Therapeutics	Imaging	Diagnostics/ Prognostics	Total	Funded
CA08-021	2009	Sep 2008	11	12	0	23	→ 2
		Feb 2009	9	10	0	19	→ 4
CA10-009	2010	Mar 2010	8	10	8	26	→ 4
CA11-002	2011	Apr 2011	5	7	7	19	<i>Pending review</i>

Program recommends reissuing the RFA each year for the next three years, with two receipt dates per year

Ten Bridge Awards: FY09/FY10



Ten Bridge Awards: FY09/FY10



FY	Company	Technology/Product	Award Size
2009	Lpath Therapeutics	Humanized monoclonal antibody for treatment of prostate cancer	\$3,000,000
2009	Optosonics	Photoacoustic CT for preclinical molecular imaging	\$2,997,247
2009	Guided Therapeutics	Fluorescence/reflectance spectroscopy for detection of cervical cancer	\$2,517,125
2009	Koning Corporation	High-performance breast CT as diagnostic adjunct to mammography	\$2,986,453
2009	Gamma Medica-Ideas	Molecular imaging to detect metabolic activity of breast lesions	\$3,000,000
2009	Altor BioScience	Tumor-targeted immunotherapy for treatment of p53-positive cancers	\$2,969,291
2010	20/20 GeneSystems	mTOR companion diagnostic assay	\$2,750,000
2010	Advanced Cell Diagnostics	<i>In situ</i> RNA detection assay for analyzing circulating tumor cells	\$2,996,450
2010	Ambergen	Expression-based prognostic assay for recurrence of colorectal cancer	\$2,998,830
2010	Praevium Research	High-performance imaging engine for optical coherence tomography	\$1,180,420

Total \$27,395,816



2 therapeutics
5 imaging technologies
3 diagnostics

Third-Party Investment

Cumulative for Ten Bridge Awards (FY09/FY10)



**Sansar Capital
Management LLC**



enlight
biosciences



THORLABS

MORNINGSIDE



Traditional VC	\$21,500,000	34%
Strategic Partners	\$24,200,000	38%
Other Investment Firms	\$5,500,000	9%
Individuals & Others	\$11,750,000	19%

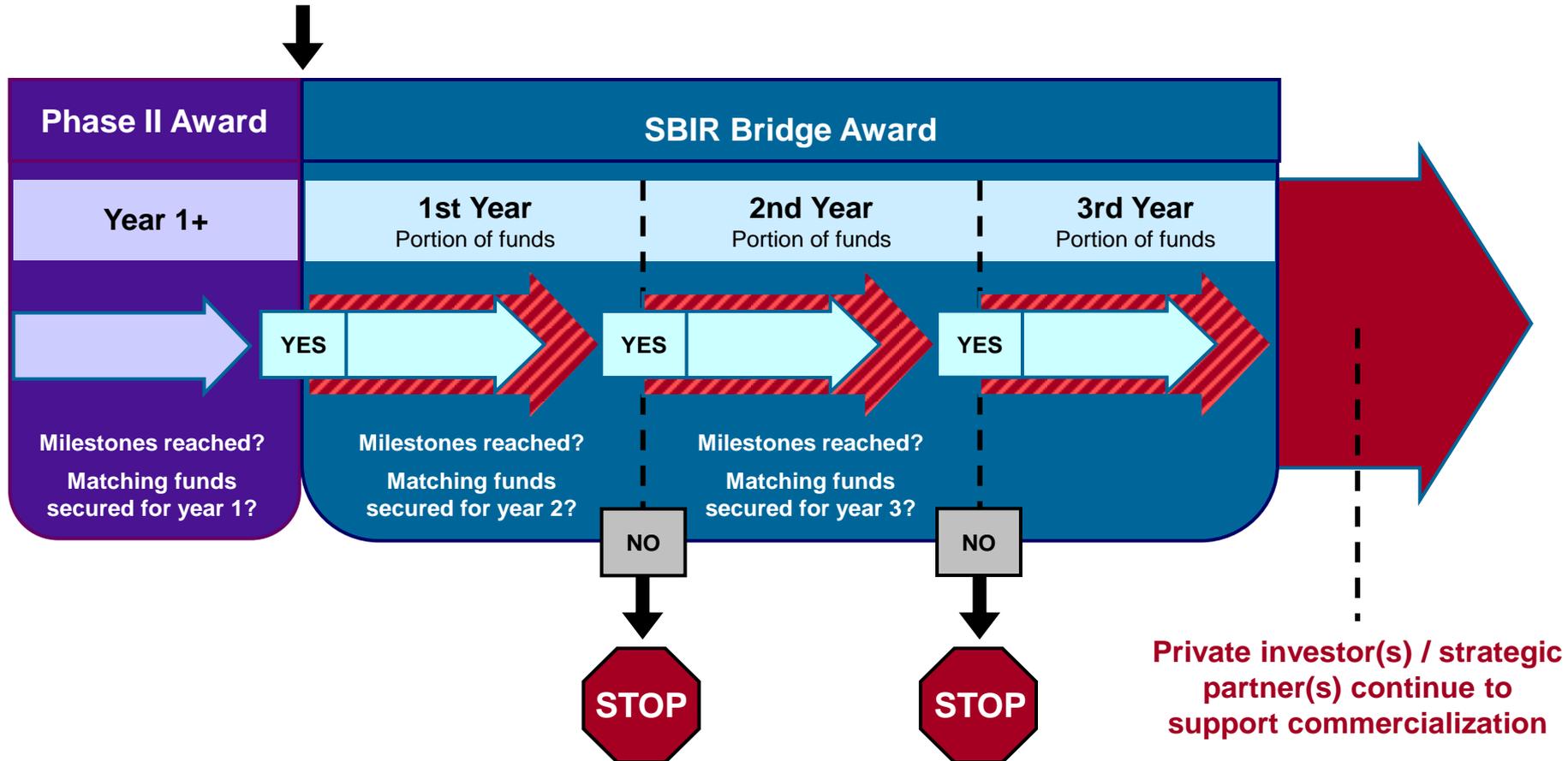
Investor Total \$62,950,000

NCI Total \$27,395,816

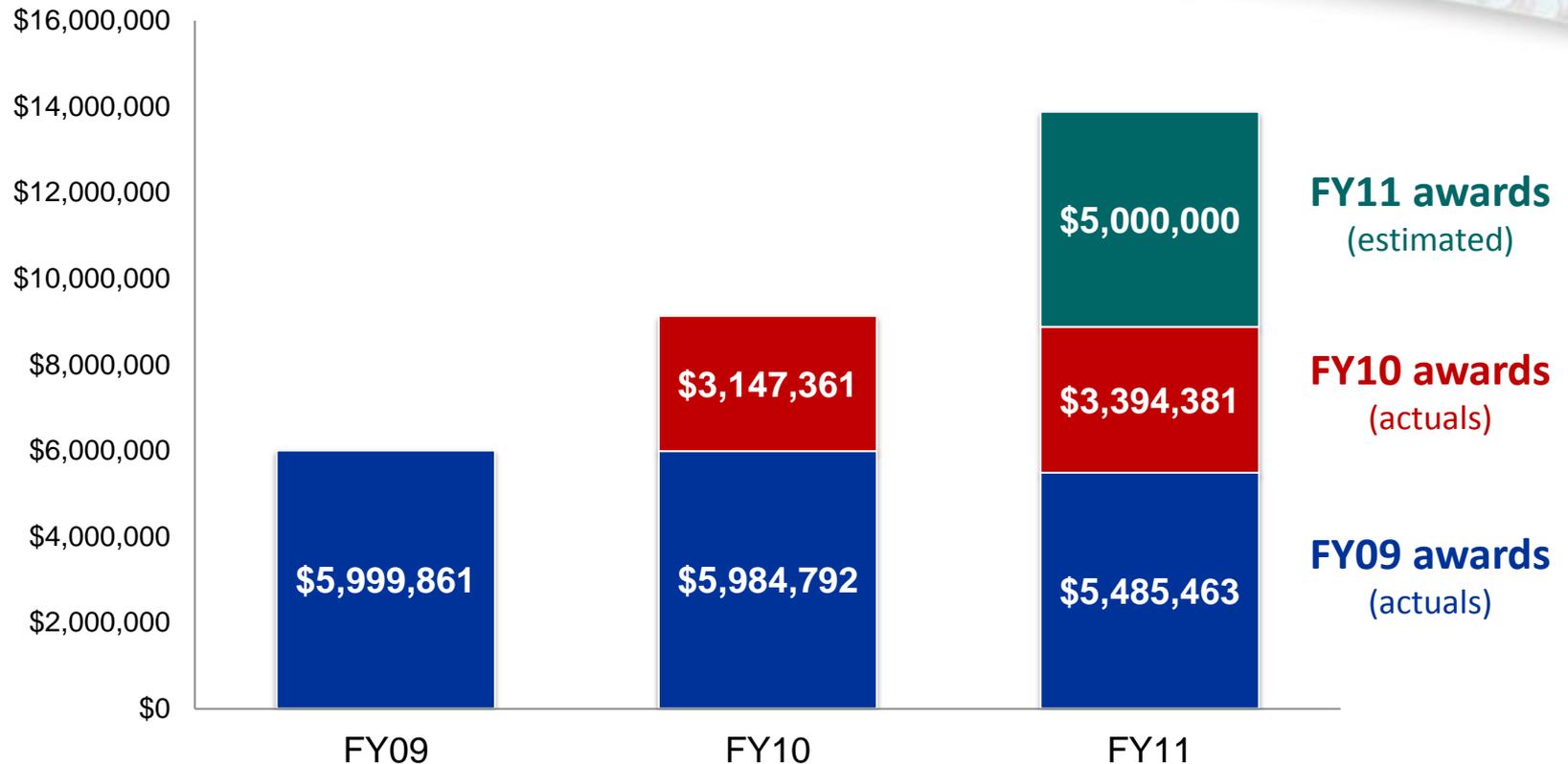
Leverage > 2 to 1

Milestone-Based Awards

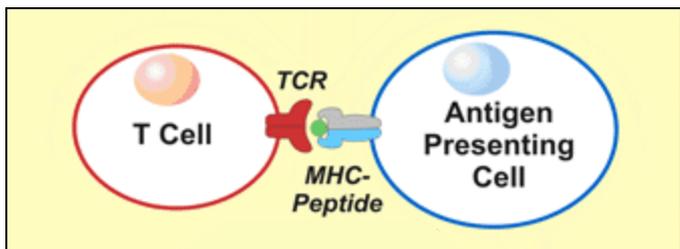
Ability to raise matching funds is a component of the Phase II Bridge Award



Bridge Award (Pilot Phase)



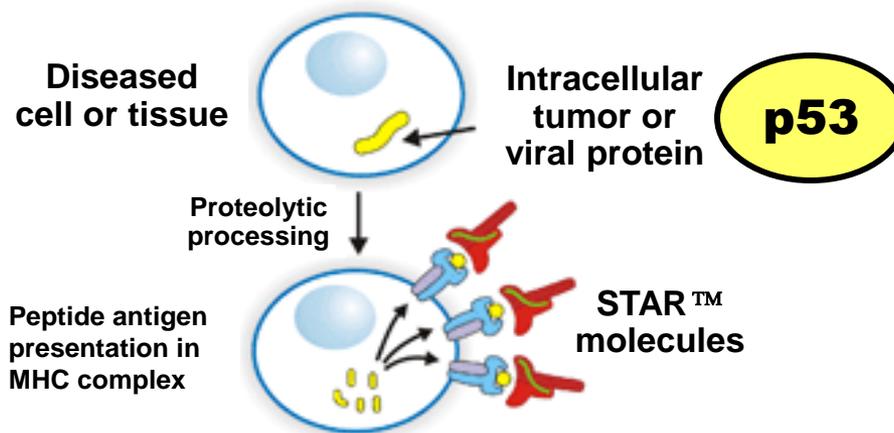
NCI SBIR set-aside	\$97.1 M	\$98.8 M	~ \$98 M
Bridge funding	\$6.0 M	\$9.1 M	~ \$14 M
% of total SBIR	6.2 %	9.2 %	~ 14 %
	(actuals)	(actuals)	(estimated)



Major histocompatibility complex (MHC)

T-cell receptor (TCR)

STAR™ ≡ Soluble T-cell Antigen Receptor

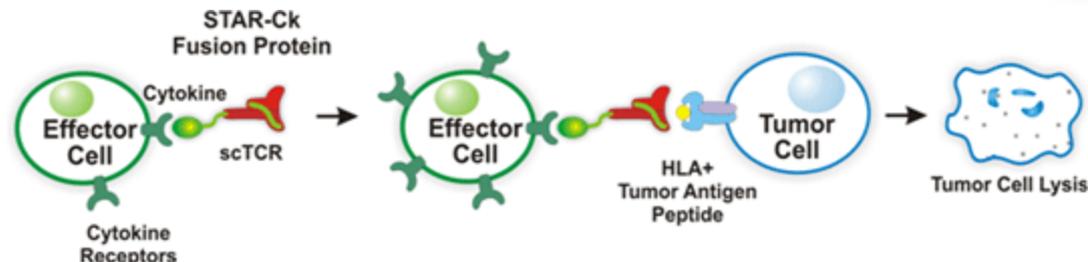


STAR™ molecules target disease-specific antigens

Drug ≡  IL-2

(ALT-801)

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](https://clinicaltrials.gov/ct2/show/study/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

PureTech Ventures

Enlight Biosciences

Endra

Newco 2

Etc.

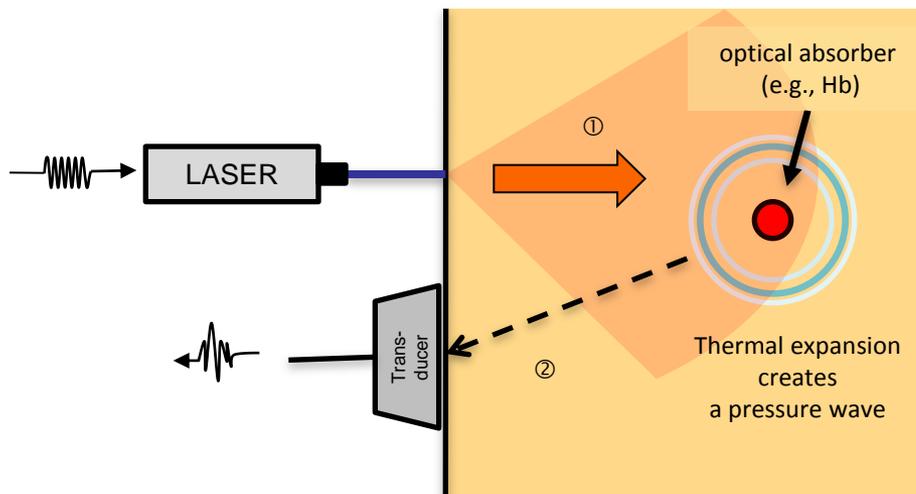
OptoSonics

NCI: \$3M

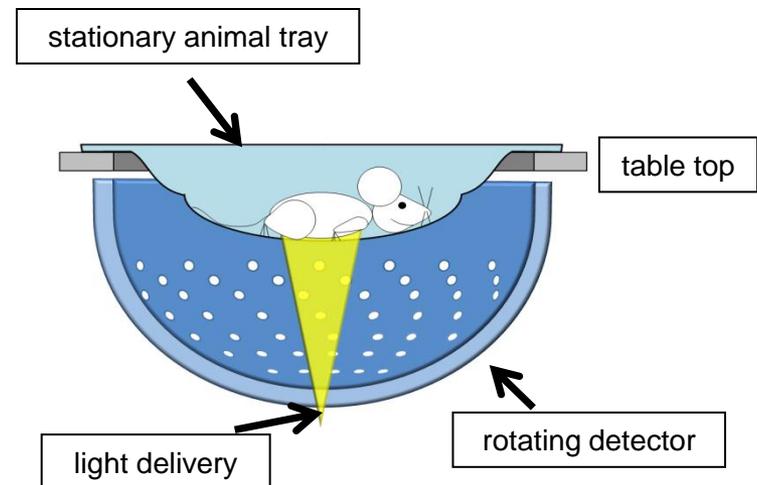
Endra: \$3M

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



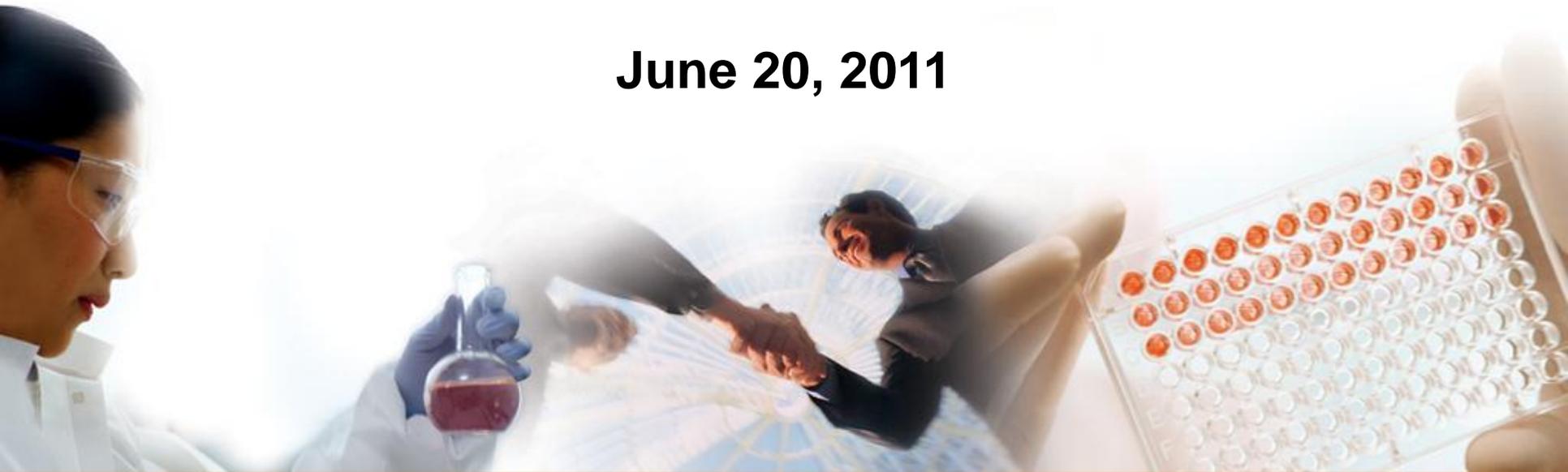
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Program Evaluation, Looking Ahead

Summary

Applications Received Feb 2009

Peer Review Rank	Score	Grant Number	PI
1	148	2R44CA110149-03	Bambot
2	154	1R44CA143716-01	Wagenaar
3	159	2R44CA097550-05A1	Wong
4	171	2R44CA103236-05A1	Ning
5	223	2R44CA091392-06A1	Sarvazyan
6	240	2R44CA140389-04A1	Burdette
7	249	2R44CA109850-08A1	Spaulding
8	258	2R44CA115205-04	Mattern
9	258	2R44CA101573-04A1	McNichols
10	261	9R44CA095930-06A1	Monticello
11	294	9R44CA119502-04A1	Stefansic
12	305	2R44CA110227-06A1	Kleerekoper
13	319	2R44CA089959-05	Oraevsky.
14	321	2R44CA096025-06A1	Fakhrai
15	Unscored	2R44CA085097-06	Conway
16	Unscored	2R44CA094566-04A1	Morgan
17	Unscored	2R44CA096409-04	Hansen

Funded

Not funded



Long-term, how do the outcomes for funded Bridge Award projects/ companies compare to those that missed the cut?