NCI SBIR BRIDGE AWARD

NCI SBIR Bridge Award

RFA Concept Review

Request for 5-year Reissuance

Presented to

BSA

Presented by

Todd Haim, PhD

NATIONAL CANCER INSTITUTE
SBIR
DEVELOPMENT
CENTER

Congressionally Mandated Programs

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❖ Small Business Innovation Research (SBIR)

Set-aside program for small business concerns to engage in Federal R&D with the potential for commercialization

Federal agencies with an extramural R&D budget > $100M

❖ Small Business Technology Transfer (STTR)

Set-aside program to facilitate cooperative R&D between small business concerns and U.S. research institutions with the potential for commercialization

Federal agencies with an extramural R&D budget > $1B

Set Aside

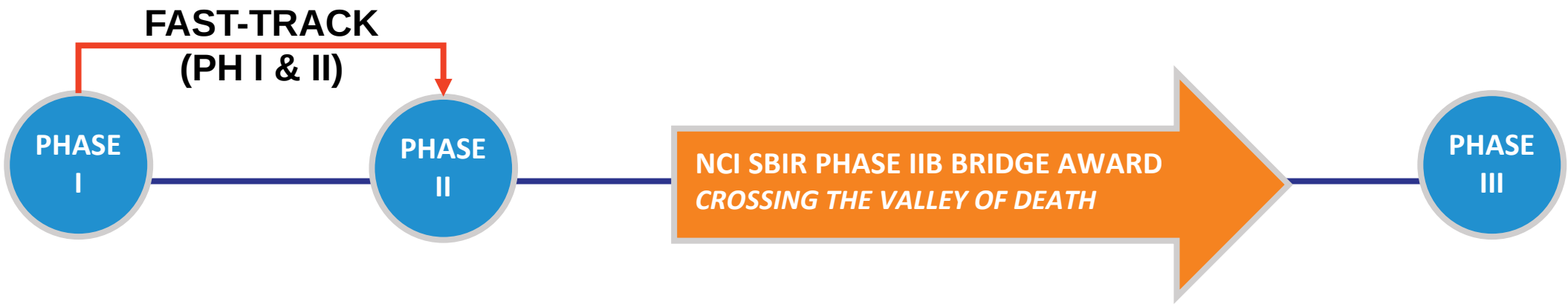
FY09	FY17
2.5%	3.2%
0.3%	0.45%

~$982M in FY17 at NIH

~$159M in FY17 at NCI

(SBIR = ~$139M)

Bridge Award = Competing Renewal Program for SBIR Phase II Awards



- Proof-of-Concept
- **Up to $300,000 over 6 to 12 months**

- Research & Development
- Commercialization plan required
- **Up to $2M over 2 years**

- Technology validation & clinical translation
- This program at the NIH was started by NCI in 2009 and has since been adapted by NHLBI and NINDS

- Commercialization stage
- Use of non-SBIR/STTR funds

* Note: Actual funding levels may differ by topic.

Public-Private Partnership

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Benefits to the NCI

- 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

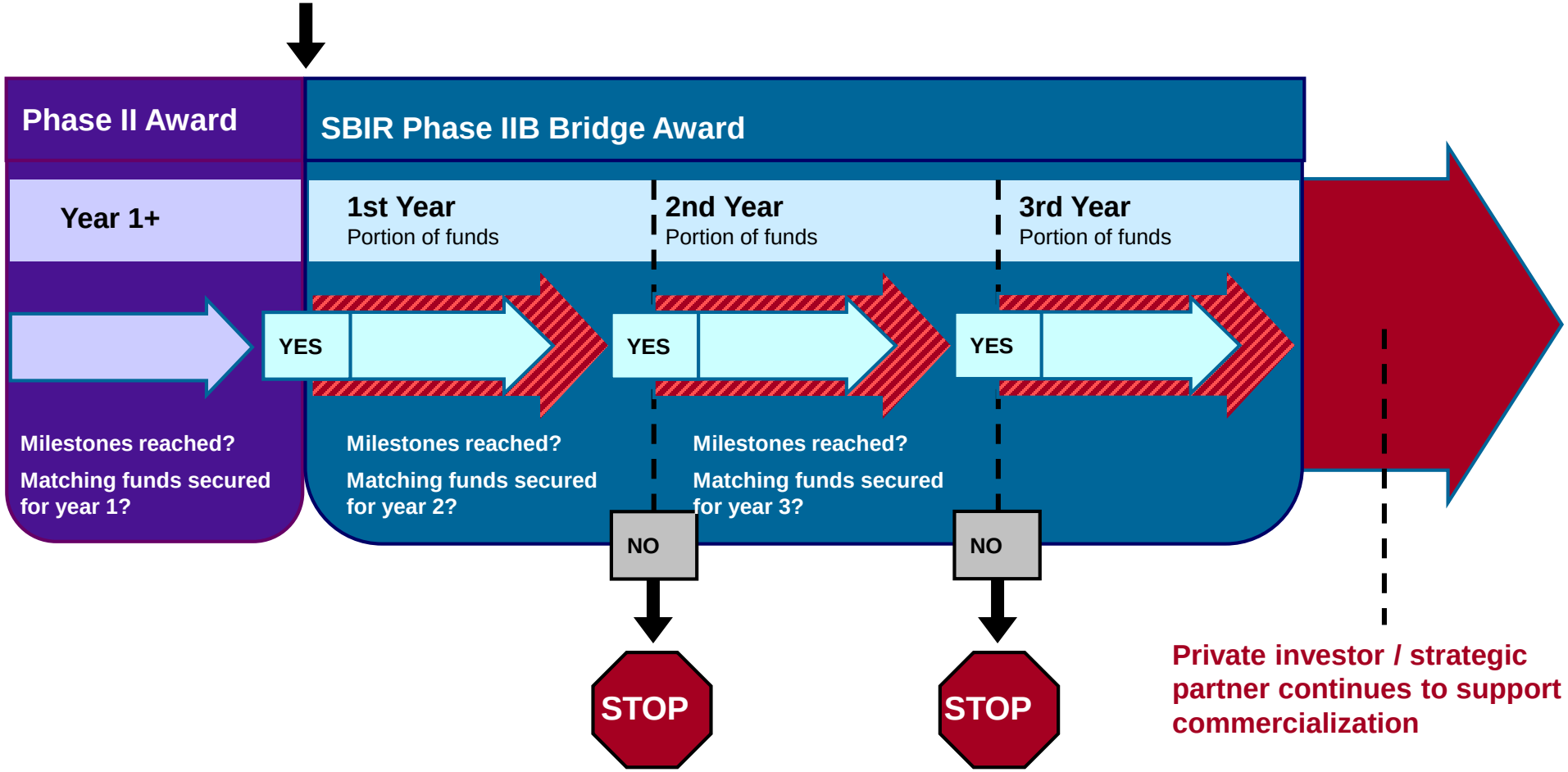
Benefits to third-party investors

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

➢ **Opportunity to share in the early-stage investment risk with the NCI**

Milestone-Based Awards

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



Valley of Death: *Moving Target & Technology Specific*

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Applicants must provide a concise "Statement of Need". This statement is expected to provide answers to the questions listed below:

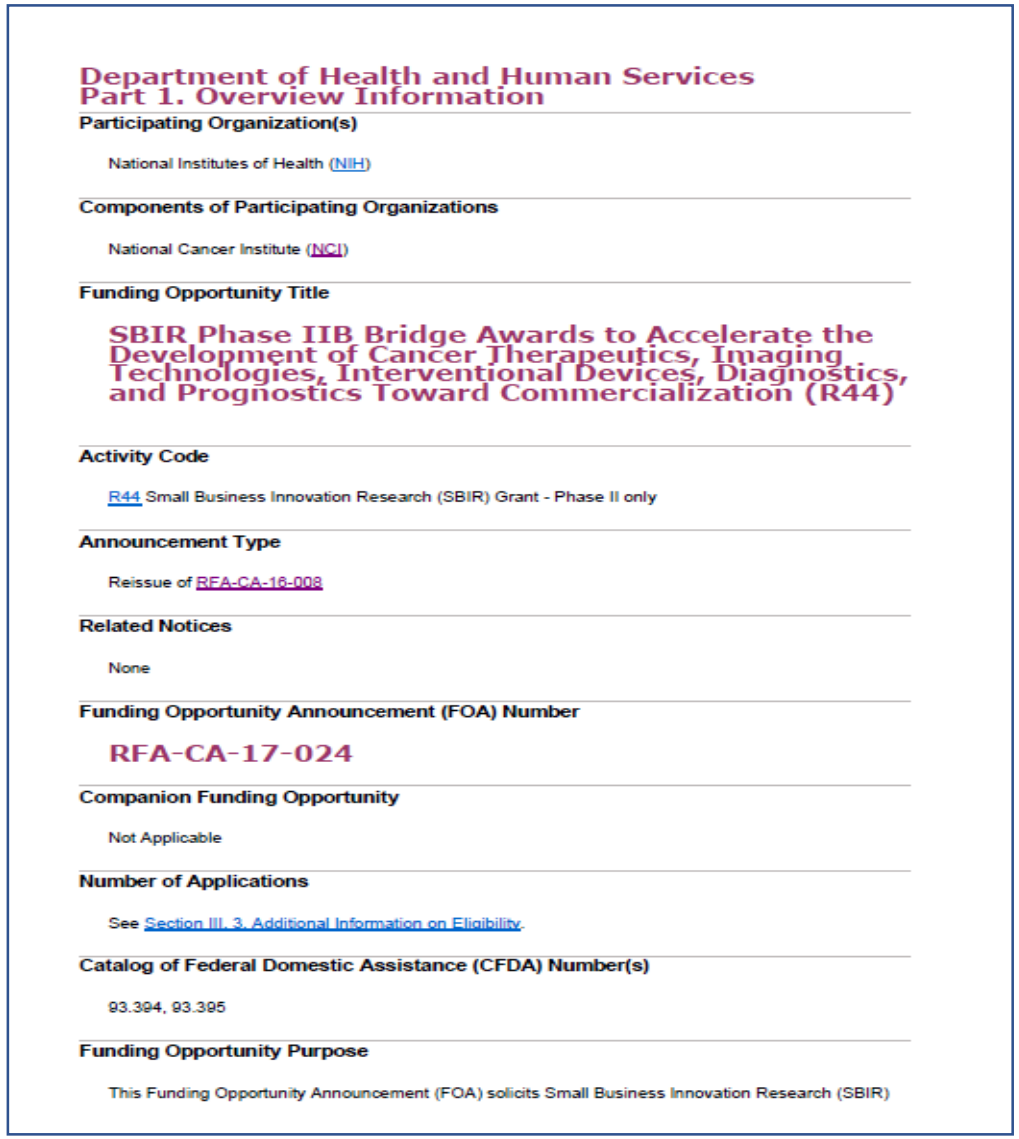
- What is the perceived "Valley of Death" for the product/technology under development?

- Why is additional government funding critically needed to accelerate the development of the product or technology toward commercialization? Specifically, what activities are being proposed under this FOA 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 under this FOA advance the product or technology far enough to attract sufficient, independent third-party financing and/or strategic partnerships to carry out full commercialization?

RFA-CA-17-024

- **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***
- **Technical Scope Limited to ~80% of NCI SBIR portfolio (* expansion recommended)**
  - Technologies requiring regulatory approval: therapeutics, imaging and devices, diagnostics
- **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
- **Recommended RFA: Clinical Trials Optional**



Department of Health and Human Services
Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH)

Components of Participating Organizations

National Cancer Institute (NCI)

Funding Opportunity Title

SBIR Phase IIB Bridge Awards to Accelerate the Development of Cancer Therapeutics, Imaging Technologies, Interventional Devices, Diagnostics, and Prognostics Toward Commercialization (R44)

Activity Code

R44 Small Business Innovation Research (SBIR) Grant - Phase II only

Announcement Type

Reissue of RFA-CA-16-008

Related Notices

None

Funding Opportunity Announcement (FOA) Number

RFA-CA-17-024

Companion Funding Opportunity

Not Applicable

Number of Applications

See Section III. 3. Additional Information on Eligibility.

Catalog of Federal Domestic Assistance (CFDA) Number(s)

93.394, 93.395

Funding Opportunity Purpose

This Funding Opportunity Announcement (FOA) solicits Small Business Innovation Research (SBIR)

28 Bridge Awards Funded To Date

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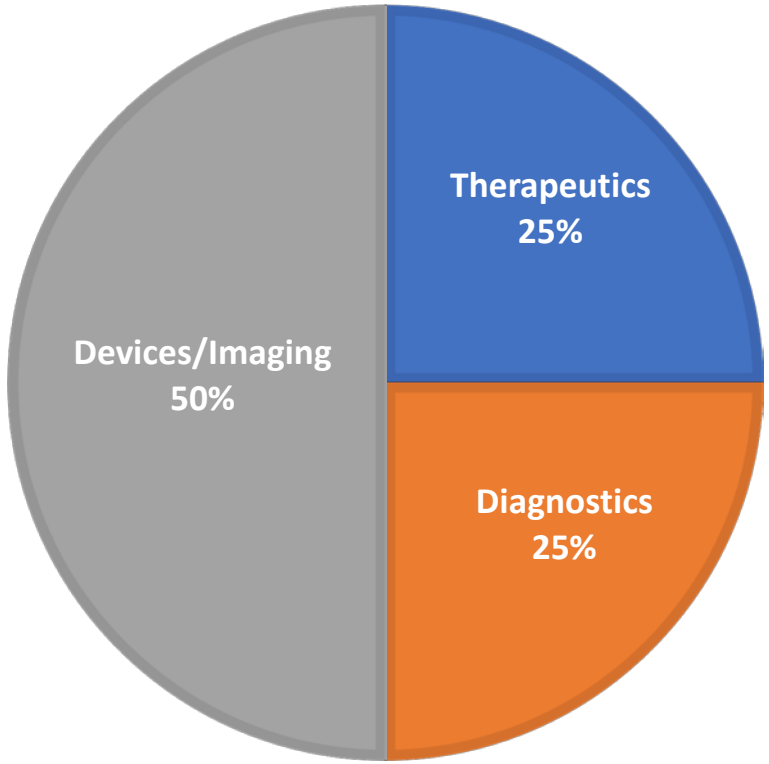
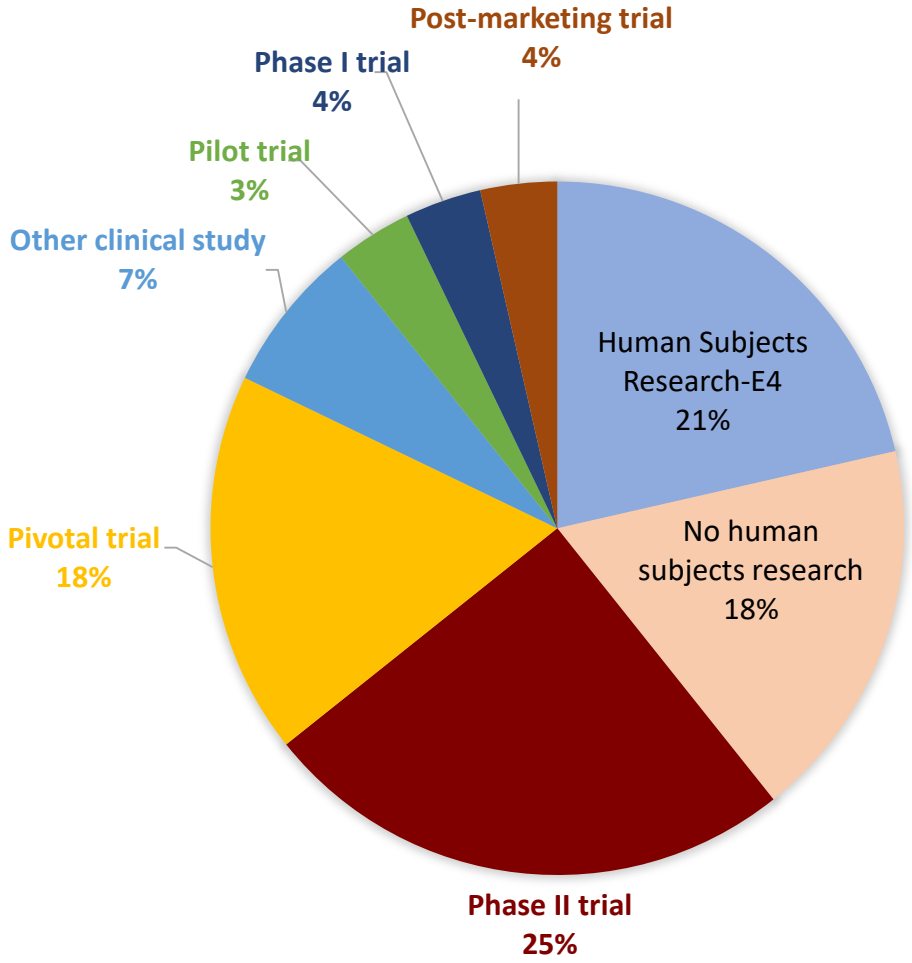
Technology Type



17 Bridge Awards included clinical trials (61%)



2017 Evaluation of the NCI Bridge Award

Evaluation Team

Mel Billingsley, CHAIR
President and CEO, Life Science Greenhouse of Central PA

Sylvaine Cases
Vice President, Oncology Scientific Innovation, J&J Innovation

Alex DeWinter
Managing Director, Healthcare Ventures, GE Ventures

Jason Cristofaro
Intellectual Property Advisor, NCI

Shannon Dahl
Co-founder, Humacyte, Inc.

Raj Singh
CEO, Vivo Biosciences, Inc.

Todd Merchak
Program Director, NIH/NIBIB

Jonathan Fleming
President & CEO, Q-State Biosciences Corp, and General Partner, Oxford Bioscience Partners.

Charge:

- A comprehensive evaluation of the Phase IIB Bridge Award program to determine if the program has successfully achieved its goals;
  - Identify strengths and weaknesses of the Phase IIB Bridge Award program;
  - Make a recommendation to NCI senior scientific leadership as to whether the program should continue;
  - Provide recommendations for possible programmatic enhancements

2017 Evaluation: Findings

3 Strengths of the Bridge Award were consistently reported in interviews with past Bridge Awardees:

1) The award was important for companies who are often at a fragile stage of growth
2) Eligibility for the Bridge Award had a positive material impact on the ability to raise matching funds
3) A relatively high-dollar award to a small business from the NIH lends a sense of credibility and further scientific validation of both the technology and company

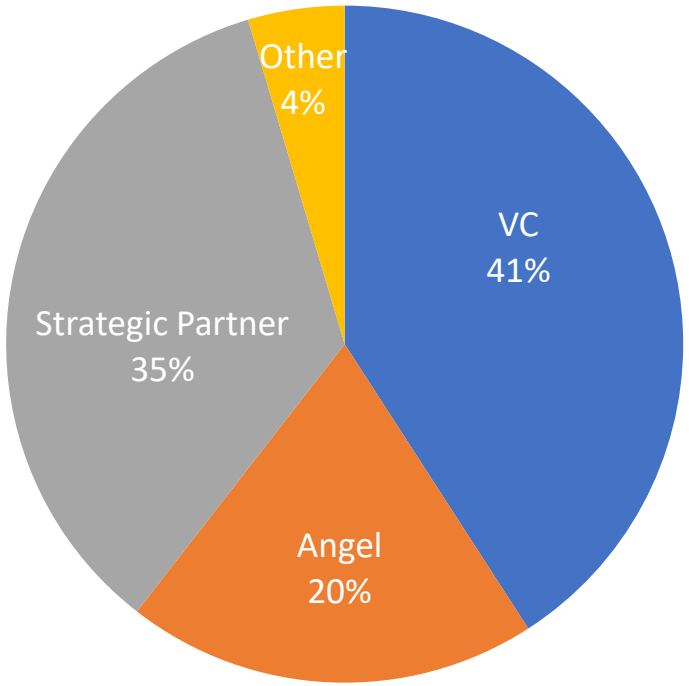
8 of the 21 Bridge Award projects funded through FY2016 have already been commercialized!

2017 Evaluation: Findings

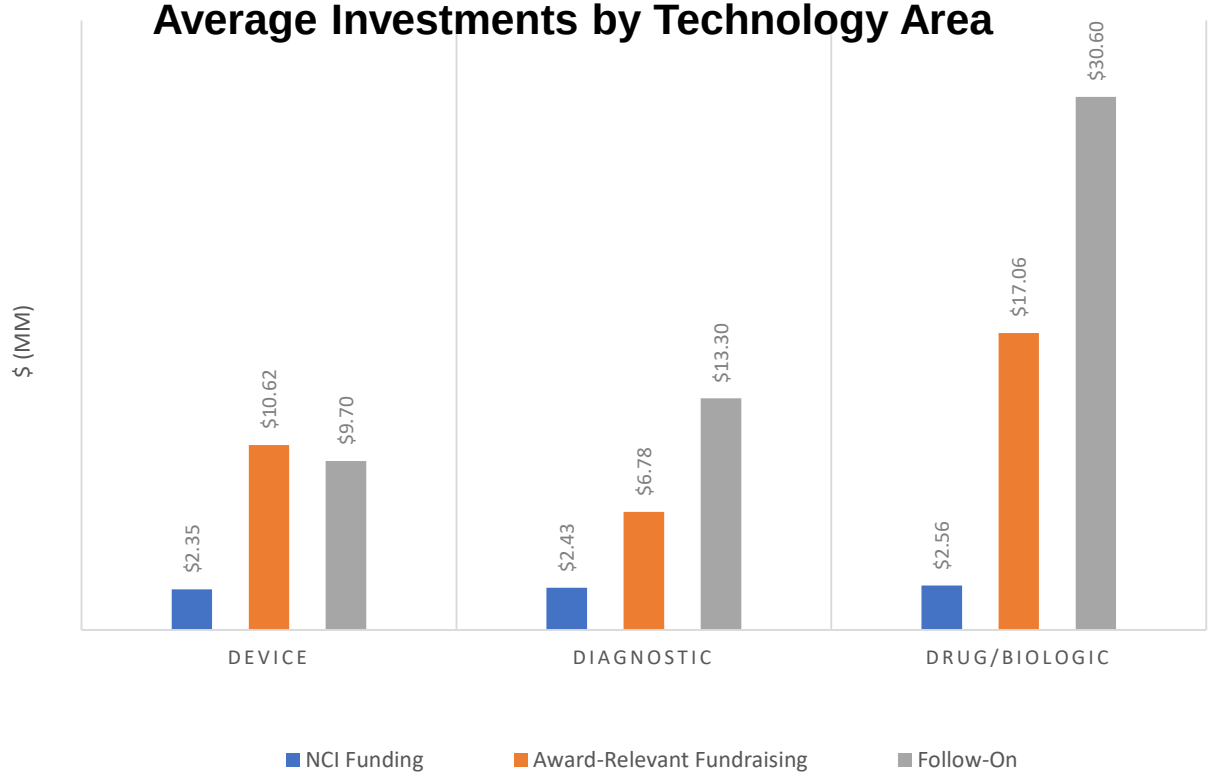
The 21 Bridge Award recipients leveraged $51M in NCI funding with ~$220M in third-party funds secured during the Bridge Award period for a ratio of:

4 third-party dollars to 1 NCI dollar

Sources of Matching Funds



Average Investments by Technology Area



Proposed Reissuance: Budget Recommendations

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- It is recommended that the budget limits be increased to a $4 million total award cap, not to exceed $2 million in any given year for up to three years.
  - Competitive preference will still be based on at least a 1:1 match with 3rd party funds and thus; may enable the awardees to further advance the proposed project and more fully meet regulatory or commercial requirements
  - The additional flexibility in yearly budgets will enable companies to appropriately devote budget as needed over the course of the project and reflect the potential differences in costs for specific tasks

- Program requests a set-aside of up to $12M in SBIR funds each year for a total of $60M.
  - It is anticipated that 5-10 Bridge Awards would be made each year up to $12M
  - This represents ~7.6% of the FY17 SBIR/STTR total budget

Proposed Reissuance: Recommendation to Expand Scope

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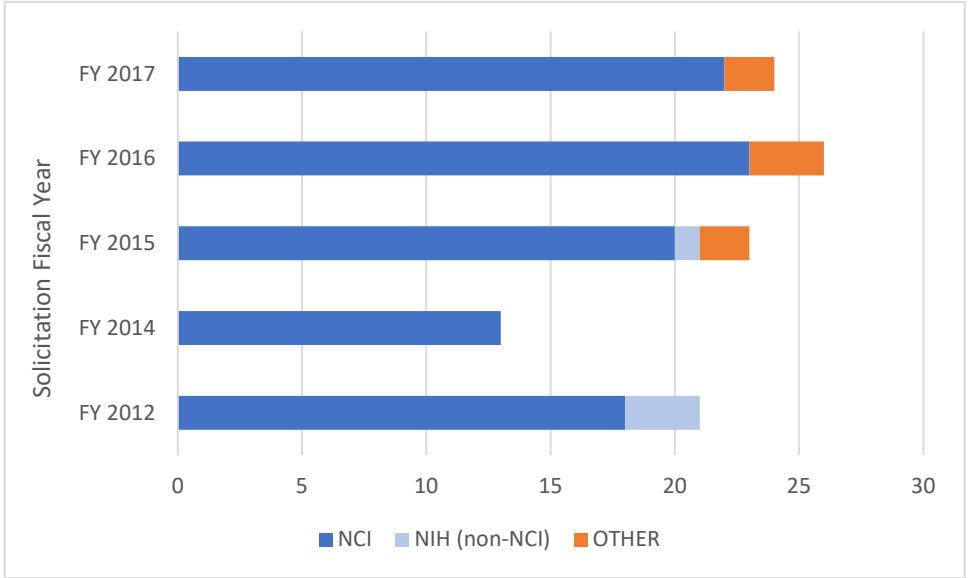
- It is recommended that the scope of eligible technologies be expanded to include all technology areas within the NCI mission.
  - The current RFA's eligibility includes ~80% of the NCI SBIR portfolio

- The NCI SBIR/STTR portfolio currently includes 5 general technical areas:
  1) Cancer Therapeutics and Preventative Agents
  2) Cancer Imaging Technologies, Interventional Devices, and In Vivo Diagnostics
  3) In Vitro and Ex Vivo Cancer Diagnostics and Prognostics
  4) **Digital Health and Software Tools for Cancer Control and Supportive Care**
  5) **Tools and Model Systems for Cancer Research.**

Proposed Reissuance: Recommendation to Increase Outreach

- It is recommended that program increases outreach efforts and awareness of the Bridge Award among potential Bridge Award applicants
  - Increased public announcements of newly-issued Bridge Awards
  - Webinars and/or workshops tailored to potential applicants featuring past Bridge Awardees
  - Expanded use of social media
  - Direct outreach to potential applicants



Efforts to expand outreach to eligible applicants with SBIR grants from other ICs and agencies have started to result in additional applications

RFA Justification

- The RFA set-aside aside funds signals NCI's strong commitment to this program and helps encourage the participation of SBIR awardees, private investors, and strategic partners
- It is important to recruit reviewers with strong industry backgrounds and business domain expertise to evaluate applications due to an increased focus and special review criteria that address commercialization strategy.

Composition of Bridge special emphasis panels (NCI DEA) versus representative SBIR/STTR panels convened by NIH CSR	Academic Reviewers Average # (Low, High)	Industry Reviewers Average # (Low, High)	Total Reviewers Average # (Low, High)	Proportion of Industry Reviewers Average % (Low, High)
Five Bridge panels convened by NCI's DEA (2012-2016)	8 (5, 12)	6 (3, 12)	14 (8, 24)	41% (30%, 55%)
Five representative SBIR/STTR panels convened by NIH CSR (2012-2016)	24 (11, 38)	7 (3, 12)	31 (19, 44)	25% (10%, 52%)

8 Bridge Awards That Have Already Been Commercialized

Company	Product	Status
Optosonics	Nexus 128 3D Photoacoustic Computed Tomography (PAT) for preclinical molecular imaging	Commercialized by Endra Life Sciences
Gamma Medica	LumaGEM™ Molecular Breast Imager	Commercialized in US and several other countries
Koning	KBCT, cone beam Computed Tomography Breast Imager	Commercialized in US and several other countries
Advanced Cell Diagnostics	RNAScope In-Situ Hybridization Technology	Commercialized, Acquired by Biotechne
Guided Therapeutics	LuViva® advanced cervical scan	Commercialized internationally
Praevium Research	MEMS-VCSEL Swept-Source Laser Engine for Optical Coherence Tomography/Microscopy (OCT/OTM) Volumetric Imaging of Tissue Pathology	Commercialized by ThorLabs
Wilson Wolf Manufacturing	G-Rex™ cell culture device to improve TIL production and reduce cost	Commercialized
Corvida Medical	Halo®, a Closed System Transfer Device (CSTD) for Chemotherapy	Commercialized

How Advanced Cell Diagnostics Leveraged the Bridge Award

Overview

- Novel multiplex nucleic acid in situ hybridization technology for single molecule detection of RNA/DNA within intact cells, providing morphological context
- Unique patented probe design (ZZ) amplifies target-specific signals but not background noise delivering clear and actionable results

• Traditional Technology is Inadequate

- × IHC (immunohistochemistry) often lacks sensitivity and specificity
- × FISH (fluorescence in situ hybridization) is limited in disease relevance
- × PCR/NGS does not provide morphological context[1] often required for accurate diagnosis, and does not fit into the existing pathology workflow, leaving pathologists out of the loop

• ACD's ISH Technology is the Solution

- ✓ Single molecule detection
- ✓ Provides morphological context[1] / broad disease relevance
- ✓ Ultimate level of sensitivity and specificity
- ✓ Highly robust and reproducible
- ✓ Degraded FFPE tissue sample compatible
- ✓ Applicable in cell and tissue
- ✓ Capable of detecting at single cell resolution point mutations and splice variants
- ✓ Seamless integration into routine pathology workflow

How Advanced Cell Diagnostics Leveraged the Bridge Award

- Bridge Award funded from 2011-2014
  - Developed a fully automated CTCscope™ assay platform
  - Validated an image acquisition system
  - Developed data analysis software
  - Initiated a 230 patient 3-center clinical study (E4: Blood Samples)
- The CTCscope™ as a part of the RNAscope® technology platform has been adopted onto existing Leica and Ventana Medical Devices instrument systems.
- Bridge Award was critical to ACD meeting technical milestones required to close $12M Series B in 2012 and helped in raising the $22M Series C in 2015

"I have been waiting for this assay for 30 years"
Mark Stoler, MD, University of Virginia

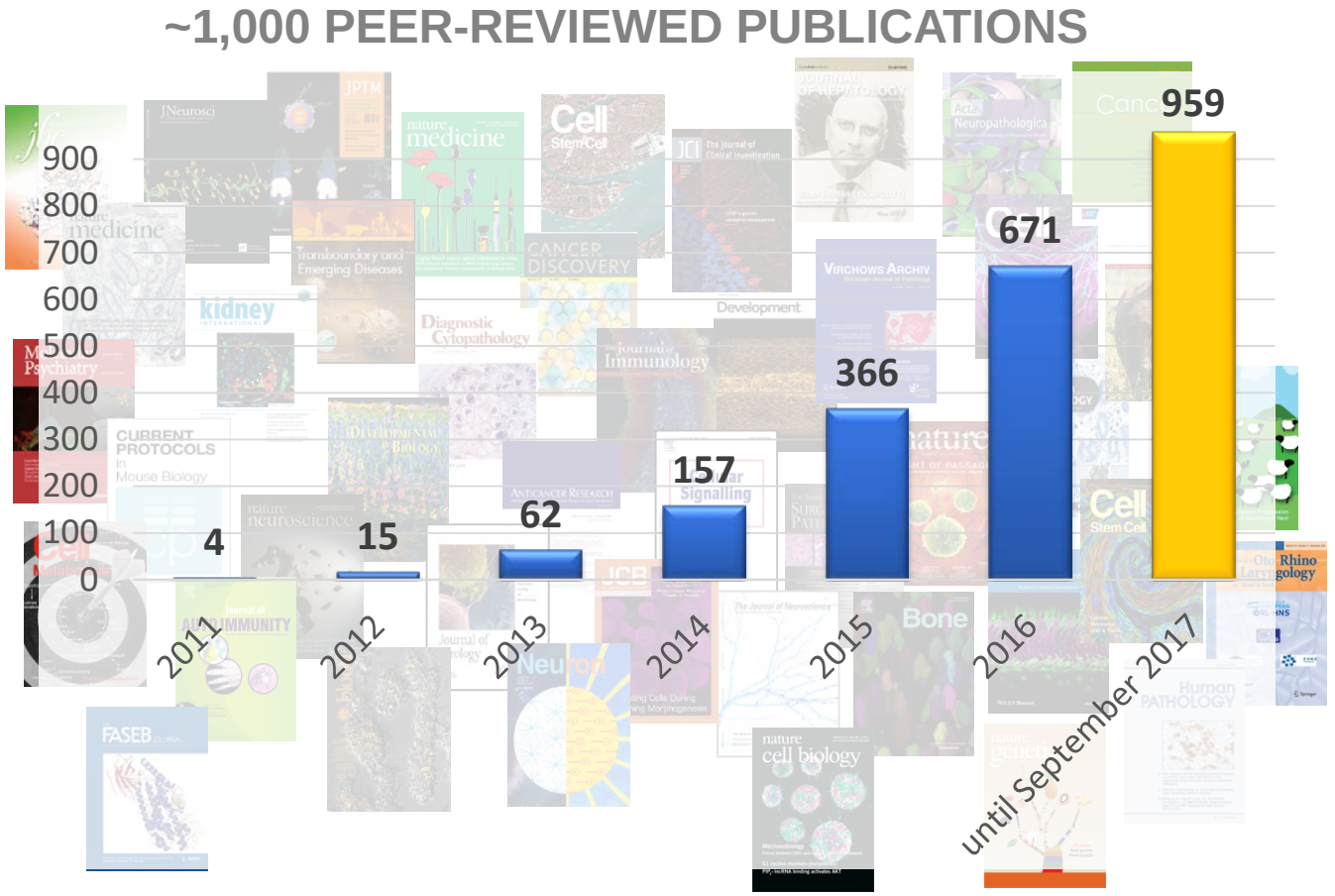
"RNAscope brings molecular pathology out of the dark into the light"
Brian Rubin, MD, Cleveland Clinic

How Advanced Cell Diagnostics Leveraged the Bridge Award

- Commercial Success post-Bridge
  - Acquired by BioTechne for $325M in 2016
  - Now over 150 employees and growing
  - Estimated 2017 revenue of $45M with industry leading growth rate of 50%

- Offers a comprehensive range of products and services based on its proprietary RNAscope® technology for research and diagnostics
  - More than 15,000 target probes
  - Manual and automated assay reagent kits
  - Diagnostic tests on market and CDx tests under development

Technology adopted by ~5,000 academic institutions and pharma/biotech companies in 40+ countries



How Wilson Wolf Manufacturing Corporation Leveraged the Bridge Award

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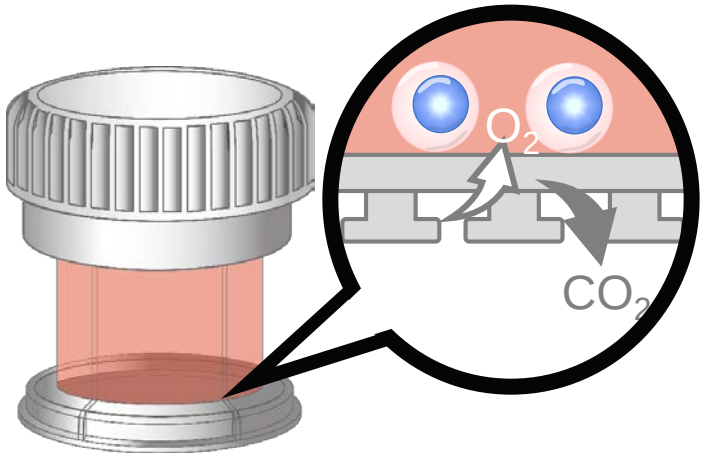
G-Rex (**G**as permeable **R**apid **Ex**pansion)

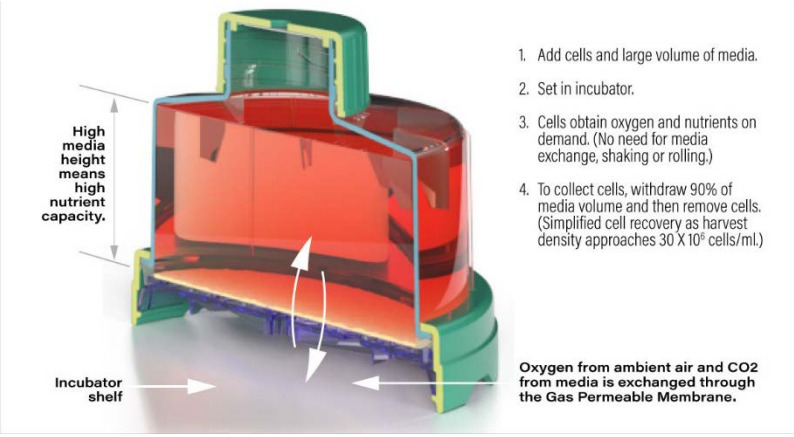
Simplified the tumor infiltrating lymphocyte (TIL) rapid expansion process from ~ 3 weeks, 170 devices and frequent feeding to **11 days, 5 devices and only 1 feeding step**

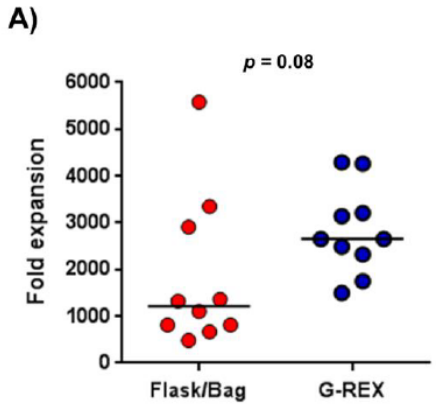


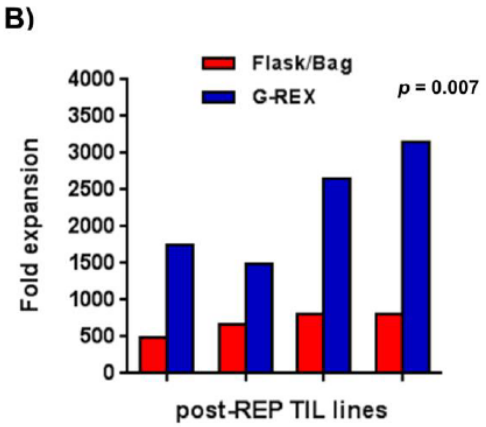
G-Rex 10

- Gas permeable membrane allows exchange of CO2 and O2
- Supports cell growth with large volumes of media
- Reduces feeding frequency and manipulation
- No rocking or stirring
- Linearly scalable products

How Wilson Wolf Manufacturing Corporation Leveraged the Bridge Award







The beneficial effects of a gas-permeable flask for expansion of Tumor-Infiltrating lymphocytes as reflected in their mitochondrial function and respiration capacity

Marie-Andrée Forget[a], Cara Haymaker[a], Jennifer B. Dennison[b], Christopher Toth[a], Sourindra Maiti[c], Orenthial J. Fulbright[a], Laurence J.N. Cooper[c], Patrick Hwu[a], Laszlo G. Radvanyi[acp] & Chantale Bernatchez[a]

- Bridge Award funded from 2012-2015
  - Refined the culture vessel to optimize surface density and support rapid expansion.
  - Optimized and tested through multiple collaborations including NCI (Steve Rosenberg and colleagues) and MD Anderson
  - Demonstrated that 100 Million TILs can be expanded to over 100 Billion cells using the G-Rex™ system
- G-Rex™ culturing devices, optimized for TIL therapy are commercially available and currently being used in seven ongoing clinical trials.
  - Resulted in successfully reducing the economic burden of producing TILs
  - The simplified TIL production platform enabled the investment community to view TIL Therapy for metastatic melanoma, cervical cancer, and squamous cell carcinoma as commercially viable
  - Facilitated the ability for Iovance (formerly Lion Biotechnology) to enter Phase 2 trials
  - Learnings from Bridge Award now being applied to other cell therapy applications and spinoff ViraCyte™

Thank You

Bridge Award Applications Received

			Applications Received				
RFA	FY	Receipt Date	Therapeutics	Devices & Imaging	Diagnostics	Total	Funded
CA08-021	2009	Sep 2008	11	12	N/A	23	2
		Feb 2009	8	11	N/A	19	4
CA10-009	2010	Mar 2010	8	10	8	26	4
CA11-002	2011	Apr 2011	4	8	7	19	2
CA12-001	2012	Dec 2011	0	2	2	4	0
		Mar 2012	2	3	1	6	2
CA12-023	2013	Nov 2012	3	2	1	6	1
		Mar 2013	1	0	4	5	1
CA14-002	2014	Mar 2014	5	3	4	12	2
CA15-010	2016	May 2015	10	6	7	23	3
CA16-008	2017	July 2016	10	10	6	26	7
CA17-024	2018	July 2017	9	10	5	24	TBD
All Applications			71	77	45	193	28

* 193 total applications were received between FY2009-FY2017. 37 of these were resubmission applications; thus, the NCI received 156 unique applications during this time.

Investment by Company