

The NCI Office of Cancer Centers Learning Series

Bringing Science to the Marketplace:

The NCI SBIR Program

Moderator: Shannon Silkensen

September 9, 2011

2:00 pm ET

Coordinator: Welcome and thank you for standing by. At this time, all participants are in a listen-only mode. This conference is being recorded and I would now like to turn the conference over to Shannon Silkensen. Ma'am, you may begin.

Shannon Silkensen: Thank you. Hello. I'm Shannon Silkensen, a Program Director in NCI's Office of Cancer Centers. Welcome to the OCC Webinar bringing science to the marketplace, the NCI SBIR program.

To ensure uninterrupted streaming of the online portion of this presentation, please close any additional windows or programs that are on your desktop. As a reminder, this Webinar is being recorded and will be archived on the Office of Cancer Centers' Website. If you have any objections, you may disconnect at this time.

As the operator mentioned, all participants are in a listen-only mode. You may submit questions in the Q&A box at any time during today's presentation and we will try to answer them during the question-and-answer session at the end of each presentation.

To find the Q&A box, click on Q&A on the top navigation bar of your screen so that a white box opens up. You can drag this box to the right-hand side of your screen if you'd like and keep it open during the presentation. After you type your question in the box, click on ask. Now for the important stuff.

I would like to introduce today's speakers, Michael Weingarten, David Beylin and Jim Olson. Michael is the Director of the SBIR Development Center and will provide an overview of the NCI's SBIR and STCR programs.

David is a Program Director within the SBIR Development Center and will offer guidance on funding opportunities and tips for applicants and lastly Jim is a full member of the Fred Hutchinson Cancer Research Center and the President and Founder of Presage Biosciences.

Importantly he is also an SBIR Program Grantee and will discuss ways to use SBIR STTR program to maximize on investment and in advanced technologies commercialization.

Remember our goal here today is to disseminate useful information **so** ask your questions and engage the speakers in conversations about the SBIR program. We're reserved about 10 minutes for questions at the end of each presentation and now Michael will begin.

Michael Weingarten: Hello, this is Michael Weingarten. I want to thank everybody for joining this Webinar today. I think it's a great opportunity for us to share information about the SBIR program. It's also very timely

because we just came out with a range of different funding opportunities that we're going to discuss today.

I'm going to actually provide an overview of the SBIR program as a whole and just some of the new things that we're doing with SBIR at the National Cancer Institute that I think would be of interest to you and also cover funding opportunities as well as some of the new initiatives we've launched such as our bridge award and then I'd be happy to answer any questions.

Following my talk then David Beylin is going to give an overview of the specific funding opportunities that we have available and again at the end of each presentation, we'd be happy to answer questions that you might have.

So why don't I go ahead and get started. So just a little bit of background information. The SBIR program stands for Small Business Innovation Research and its sister program STTR stands for the Small Business Technology Transfer program.

Essentially these are both government set-aside programs so what that means is that on an annual basis between these two programs about 2.8% of the NCI budget is set aside specifically to fund projects with small businesses.

And if you look at the total budget of the program at the NCI, it's about \$109 million this year across the NIH because every major institute at the NIH also has an SBIR program. The program is actually quite large. It's about \$650 million total across all the different institutes at the NIH.

And why are SBIR and STTR important to the NCI? Well, they're really our primary resource for enabling the commercialization of technologies, many of which have been developed initially with other funding such as R01 grants or program grants.

So if you look at the kinds of projects we fund they actually cut across much of what the NCI does. Those include small molecules and biologics, cancer diagnostics as well as cancer imaging technologies and electronic health and education tools.

If you're a small business or if you're working at a cancer center and you've got an innovation that you're considering either partnering with a small business on or maybe starting your own company, why should you have an interest in SBIR or STTR funding?

Well, today it's actually probably the largest source of early-stage funding for start-up companies in the country. That's particularly true with the economic downturn. A lot of the other sources of funding for startups has really dried up so many times we're the first source of funds that a small business will look towards other than friends and family.

But we're many times the very first source of funding that a company will look towards when they're just getting a company started and they're trying to develop a technology that has applications in the cancer area.

The other important thing is that our funding is stable and predictable. Our budget has actually been in the \$110 million range over the last five years now so it's a source that you can rely upon.

Other important aspects to the program include the intellectual property rights are retained by the small business concern. If you apply to this program, you're either applying for a grant or a contract so it's not a loan.

There's no repayment required under the program and in terms of your company, it doesn't impact the stock or shares in any way. There's no dilution of capital because the NCI does not take an equity position in your company.

Other things, because all grants are contract applications you submit go through the typical NCI or NIH peer review process, the fact that if you do well in peer review and we do fund you under a grant or a contract, that will help provide your company with additional recognition and visibility particularly, on the technology side, and that can really be helpful in terms of trying to raise additional funds from other parties down the line.

So it can be a really nice tool to help you raise funds from venture capital or for other strategic partners too. A little bit of background on eligibility. In order to apply for an SBIR, you do have to be a small business operating here in the United States and you have to be headquartered here in the United States.

You have to be a for-profit U.S. business. The other rules include a requirement that there be 500 or fewer employees and the company

itself must be at least 51% owned by U.S. individuals and independently operated or at least 51% owned and controlled by another business concern that is itself is 51% owned and controlled by one or more individuals.

The other key requirement is that the PI's primary employment must be with the small business concern at the time the award is made so sometimes we have companies, you know, in a startup situation.

They apply, they're a brand new firm. Maybe the company isn't up and running at the time that they apply but at the time the award is made, the PI and the company have to be ready to go and the PI's got to be primarily employed by the small business concern.

The sister program again to SBIR is the STTR program that has the same rules that I just went through but also some additional rules and those include that the whole purpose of the STTR program is to facilitate the transfer of technologies from a U.S. research institution - typically that's going to be a university or a federal research and development center.

The goal of the STTR is to have this partnership between the U.S. research institution and a small business which would involve an intellectual property agreement also between both organizations and the goal is to transfer that technology to the small business and to use STTR as a funding vehicle for helping move that technology towards commercialization.

One of the nice aspects of STTR is that the principal investigator's primary employment can be with either the small business concern or

if the PI would like to stay at the research institution, that is also possible under the STTR program.

SBIR and STTR are both three-phased programs so Phase 1 is typically a feasibility study. Usually it's a six to 12-month project and in terms of average funding it ranges typically between \$150,000 and \$250,000 in funds.

If that project is successful then you are invited to apply for a Phase 2 award, which would be a follow-on to the Phase 1 and that's for the full research and development of the technology. Typically the average dollar size of a Phase 2 award is one to \$2 million and a two to three-year timeframe.

We do at the NCI we do cap award sizes at \$2 million for Phase 2 awards so you do have to stay underneath that cap. One critical aspect to your Phase 2 application is that a commercialization plan is required as part of that application and it's one of the key criteria in terms of the review of the overall proposal.

And David's going to - when he gets into his presentation - he's going to be offering some suggestions in terms of the kinds of things you really need to be covering in your overall commercialization strategy as part of that application.

Phase 3 is the next phase of SBIR and that's actually the commercialization stage and Phase 3 actually must be funded by a small business raising funds from other sources other than SBIR so SBIR funds don't actually go to the direct commercialization of the technology being developed.

Just a little bit of an overview of our portfolio before I dive into an overview of kind of how our different funding opportunities work and on average we fund on the order of about 450 to 500 projects on an ongoing basis.

Those are Phase 1 and Phase 2 projects and that's what this slide will show you and as you can see, therapeutics actually represents the largest part of our portfolio at 31% of all the projects and that includes small molecules which would be the largest category in terms of funds and numbers of projects followed by biologics and then nanotechnology-based therapeutics.

Second-largest category in terms of our portfolio is in the area of diagnostics specifically in vitro diagnostics and that's at 24% and that's then followed by imaging technologies and then areas such as devices for cancer therapy.

We have a number of different solicitations. The first one for those who have applied before, the one that's most commonly known is what's known as the SBIR Omnibus Grant Solicitation. That is released in January of every year with three different receipt dates and essentially it's an investigator-initiated solicitation.

It's really a catch-all solicitation where you can propose in most topic areas as long as they're appropriate for the institute that you're applying for so obviously for NCI we're going to be interested in cancer-focused applications with commercial opportunity.

That solicitation has three different receipt dates, April, August and December. We also come out with other program announcements. These are grant-based announcements throughout the fiscal year and if you're interested in just seeing some of our different funding opportunities, I'd encourage you to go up to our website which is <http://sbir.cancer.gov>.

And then what we're really going to be focusing on today are our contract funding opportunities. That announcement was actually just released one week ago with 12 different opportunities and those proposals are actually due on November the 7th.

And again that's our website, <http://sbir.cancer.gov>. You can get all the information that I'm discussing today and also the specific funding opportunities regarding the program. In addition you can sign up for updates on our website.

If you do that anytime that we come out with a new funding opportunity, you'll automatically get information on that if you're signed up to do so. Want to get into one other new program that we just launched two years ago. We call it our Bridge Award program. I went through the three phases of SBIR a little bit earlier. This is actually a new program.

The bridge kind of falls in between Phase 2 and Phase 3 and the whole goal of the bridge program is what we found under the SBIR program is that on average companies if you were to look at average funding levels for companies who had received Phase 1 and Phase 2 SBIRs and it typically ranged between one and one-and-a-half million dollars.

The goal of the bridge is to actually help fund companies across what is commonly known as the valley of death where we found a number of our companies were getting promising initial data with Phase 1 and Phase 2 SBIRs but they really weren't - they didn't have enough - funding to get a critical amount of data to then be able to go out and raise funds from the private sector.

So the whole goal of the bridge program is that at the NCI we offer an additional award under the bridge where we will share in the investment risk with other investors.

The way it works is that with the bridge program companies, small businesses who are Phase 2s are allowed to apply under this program and we will give competitive preference and funding priority to those applicants that are able to raise third-party matching dollars to match the investment that they're looking for from the NCI.

So the amount of funding that you can apply for under the bridge is up to \$3 million total. It's \$1 million per year for up to three years. It's available to current Phase 2 grantees or contractors and also those awards that ended within the last two years.

In terms of matching dollars, those funds can come in terms of either a cash investment from a third-party investor; it could also be funds from a strategic partner such as big pharma and this just gives you a real-life example of how the bridge program actually works.

If you look at the way we've drawn this on the chart, you look at typical Phase 1 and Phase 2 dollars and you look at an example of a

therapeutic project, Phase 1 and Phase 2 dollars are enough funds to take a project many times about half the way through preclinical development and at that point many of our companies were running out of funding.

So with the bridge program we provide the opportunity for companies to then apply for an additional \$3 million in funds and the goal of the bridge is to help also pull private investors in at a much earlier stage of investment so again it's a partnership between the NCI and a third-party investor to actually help co-fund these projects with small businesses in our portfolio.

These are all milestone-based awards so companies are required to have matching funds each year that they would be funded that would match the NCI investment and also we monitor these awards very closely in terms of technology milestones being met.

We've ran this program over the last two years. A total of 10 projects have been funded. This slide just gives you a little bit of an overview of those 10 projects and as you can see, two are in the area of therapeutics, five are in the imaging area and three are in the diagnostics category.

The other key thing that we've really done under our program is really change the way that we manage SBIR and establish really a new paradigm for managing SBIR at the NCI. We've set up a center whose only purpose is really to spend 100% of their time working with small businesses and managing these projects.

As you can see, we have a total of 10 program directors, all primarily with industry expertise and they're available really to advise small businesses on the outside in terms of how to apply the program and then to manage and help mentor these companies as they develop their technologies. Another key program that we launched we call our NCI SBIR investor form.

It's another program that we offer in which we help connect companies that we are funding through SBIR with the investment community as well as potential strategic partners such as large pharmaceutical companies and we actually showcase the top companies in our portfolio to the investment community.

We do this one day during the year. We actually held our last event last November in San Francisco and this is really an opportunity to help us connect some of our best companies and help them raise these additional funds so that's my presentation. I'd be happy to answer any questions.

Shannon Silkensen: Thank you, Michael. We received a couple of questions over the chat line during your presentation and I guess I'm just going to read you a couple of them now. Somebody asked if they receive venture capital funds that cover them during sort of Phase 1, are they eligible to apply directly for Phase 2 funding?

Michael Weinstein: Actually you can't skip phases under SBIR. You have to come in initially as a Phase 1 but what you can do is for many of our projects or many of our solicitations you can submit what's called a fast-track application which is a combined Phase 1/Phase 2 application.

So you could take all the preliminary data that was generated from the venture capital funds that you already raised and then apply for the development of the technology, include all that information in your proposal whether you submit another, you know, a Phase 1 proposal to the NCI or this fast track that I mentioned.

And whether we accept fast tracks on any specific funding opportunity will be outlined in the specific solicitation that's available.

Shannon Silkensen: Someone else was wondering if the bridge funding was restricted to the NCI or does it apply to the other NIH institutes as well?

Michael Weinstein: At the present, NCI is the only institute that currently offers the bridge program; however, I can tell you we've worked closely with a number of the other institutes at the NIH and they've all expressed a lot of interest in this program just based on the success that NCI has had.

And two other institutes are looking at implementing the same program, one being the National Heart Lung and Blood Institute and also NINDS is also looking at launching a similar program too.

Shannon Silkensen: Somebody was asking if a company submitting under the Omnibus grant proposal could team up with another company to perform part of the project?

Michael Weinstein: Yes, so that's an excellent question. Yeah, actually the way SBIR is structured under Phase 1 applications you can outsource - you as a small business - can outsource about a third of the dollars to other

parties. That other party could be academic institution or it could be another business whether large or small so that is allowed.

Under Phase 2 you can actually outsource approximately half of the dollars to another party, again whether an academic organization or another company.

Shannon Silkensen: Great. Michael does NCI fund therapeutics that are targeted towards the side effects of cancer treatment?

Michael Weinstein: Yes, yes, we do. We have funded projects in that area.

Shannon Silkensen: Great. Somebody else was asking can they be the PI on both an R01 grant and an SBIR grant at the same time?

Michael Weinstein: Yes, that is possible as long as the individual has the time allocated where they can actually - they have enough time - to actually spend on both projects. The other key thing is you want to make sure that there's not a direct overlap in terms of the projects, your R01 grant and your SBIR grant. These should be - the scope of the work and the aim - should be different from both projects.

Shannon Silkensen: So Michael is there actually a minimal effort or a budget for a researcher to be on an STTR grant?

Michael Weinstein: Minimum effort for a - actually that's a good question. Do you know the answer to that, David?

David Beylin: I think 10%.

Michael Weinstein: Yeah, I believe the minimum there is you have to allocate at least 10% of time, at least the PI would have to be able to allocate at least 10% of their time to a project.

Shannon Silkensen: Great, and we just have time for maybe two questions. There's also a question would be Michael can you explain a little bit about how the NIH technology transfer works and how they can gain more information about this?

Michael Weinstein: Yeah, so I think what the questioner's asking here is David's going to delve into our contract topics that are currently open for competition and actually there are two technology transfer topics that are included this year.

And essentially these are technologies that were originally developed by the NCI in our own labs and that we are making available to license to a small business so these are fully describe in the contract solicitation but we're actually going to be putting together a Webinar just on the technology transfer topics to really get into the details of those.

And whoever asked that question, if you just shoot us an e-mail directly after this Webinar, we'd be happy to follow-up with you in detail.

Shannon Silkensen: Great, and Michael just the last question we had, is it encouraged for a company to cooperate with an academic institution?

Michael Weinstein: It really depends on the specific case of the company. You know, we cover startups with this program. We also have small businesses that

are more mature and more advanced that are doing their own technology development efforts internally.

So if you're a startup, if you're looking to tap into expertise and that expertise is really best available in an academic institution, then I would encourage it but, you know, there are other ways that you can do this too including collaborations with other companies so it's not a requirement.

The other point I wanted to make regarding the PI's time is that for SBIRs the PI has to be spending at least half of their time with the small business, you know, in terms of eligibility for an SBIR.

Shannon Silkensen:

Great, Michael, thank you for all of that. We're now going to transition to David Beylin who will offer guidance on funding opportunity and tips for applicants.

David Beylin:

Good afternoon, good morning for those on the West Coast. It's a pleasure to be addressing you. I would like to discuss two different topics. One is I'll talk a little bit about our contract solicitation that Michael mentioned that just came out and I will also talk about the application tips which are mostly addressed to people who have not had prior experience with the SBIRs and it will differentiate how the SBIRs are different from the academic grants.

So first of all, we have a new solicitation announced a week ago. This is a Fiscal Year 2012 SBIR contract solicitation. It only comes out once a year and therefore if you think one of the topics is of interest, the time to consider application is now.

The funding opportunity is solicitation of NIH and CDC for SBIR contract proposals and there are topics from NCI as well as a few topics from other institutes. There is one application receipt date per year and the next receipt date is November 7.

The request for proposals can be found on the NIH Website or you can also locate it through our website, <http://sbir.cancer.gov>. NCI published 12 topics which are listed on the next slide in the areas as disparate as drugs, diagnostics, imaging, health IT and research tools. These are the titles of the 12 topics.

They have a number and they have a title and they include development of anti-cancer agents; development of companion diagnostics; radiation modulators for use during radiotherapy and reformulation of cancer therapeutics using nanotechnology; probing tumor microenvironment using in vivo nanotechnology based sensors; development of innovative algorithms for analysis of in vivo images; novel imaging agents; collection, storage, analysis and reporting systems for dietary images which would be an example of a health IT topic; development of low-cost, small-sample multiple analyzed technologies for cancer diagnosis, prognosis and early detection.

There are also two topics which Michael mentioned which are NIH specifically NCI technologies which are available for licensing and the SBIR program provides an incentive for companies to license these technologies.

And the last topic is generation and qualification of site-specific, post-translationally modified programs for use as calibrators in

pharmacodynamic assays. Three of the topics are marked with an asterisk and I will just go through each of these topics in a little more detail to give you an idea of what they're asking for.

The first example is Topic 291, radiation modulators and the budget cap for this topic is \$200,000 for the Phase 1 and a million and a half for the Phase 2. Unlike for the grants where the SBA guidelines are interpreted as guidelines by the NIH, these are hard caps so if you apply with a project outside of these limited, you may not be funded.

The number of anticipated awards in 2012 is three to five. The project goal is development of radio sensitizers, radio protectants and radio mitigators and an example of a Phase 1 work scope may include in vitro testing clonogenic survival studies and preliminary toxicity and some other activities are listed as appropriate for the project.

The Phase 2 work scope is expected to include in vivo experiments, PK and PD in rodent models and GMP drug production or sourcing if applicable and IND approval preparation.

Second example is Topic 307, imaging agents. The budget is up to \$250,000 for the Phase 1 and up to a million and a half for the Phase 2. We anticipate to make three to five awards but reserve the right to make fewer or more.

The project goal is to develop novel imaging agents for early detection of cancer, certification of patients for selecting cancer therapy, surgical planning, evolution of tumors once the chemotherapy or radiation therapy detection of cancer recurrence and other.

The work scope may include animal testing, formulation, GMP production, PK/PD, toxicological studies and other activities as appropriate. One of the topics which has been issued by NCI before and is fairly popular is companion diagnostics.

The budgets are along the same lines. We anticipate to make four awards and the project goal is to develop companion diagnostics for selecting patients for existing drugs or drugs in clinical trials to increase the safety and effectiveness profile of the drug.

The Phase 1 work scope is to test development analytical validation and we do require that if the drug is not commercial available, the company must establish partnership with the source or with a large diagnostic company. The Phase 2 work scope is the full clinical validation. If you have any questions about the contract solicitation, I will be happy to answer them.

We'll talk a little bit about what it takes to get funded under the SBIR program and there's some application tips. First of all SBIR program is highly competitive. It's competitive on the same level as the academic programs.

This hasn't always been the case in the distant past. At this point this is a very competitive program so if you think of just trying out sending the application without proper preparation, it's very unlikely it will succeed so this is most likely not good use of your time.

The commercialization potential is very important in this program and most successful SBIR projects are product-focused which really

differentiates them from the research grants. First decision is whether you want to apply for the SBIR program or not.

The SBIR application is appropriate for a startup, often an academic spinoff where there is an entrepreneur founder with experience in the field, the highly innovative technological solution solves significant clinical need, there is commercial potential, and there is need to generate initial or further feasibility to date in order to approach the private funding sources.

Maybe it's too risky for private investors at this point. There are a few comments in areas when it's not worth applying for the SBIR. Chasing solicitations for some companies is not a good use of time and money for us.

Sometimes PIs think that SBIRs are a lot less competitive than academic grants and setup a company specifically to try to get the funding. This is probably not a great idea in most cases.

We discourage applications with incremental upgrades to existing products, with "me too" products matching competitors' capabilities and products at the stage where the investment need far exceeds our funding level so if you need \$20 million to take the drug to the next level, there is not good funding source.

I'll briefly talk about this strategy for building the application and will identify the key components. These slides will be available on the Website so I will be very brief.

We expect highly innovative sound and focused sound science, well-designed studies with the Phase 1 addressing key visibility questions and Phase 2 proceeding to eliminate technology and sometimes clinical risks. Significant commercial potential and strong team supplemented by an appropriate consultant and collaborators.

The key documents to become familiar with before applying are the Omnibus solicitation, which for the grants or the RFP which I discussed for the contracts as well as the SF-424 application instructions, are a great source of information about all kinds of administrative questions.

Some of the tips for the application are that you want to start early. Strong proposals take a long time to develop, usually a few months. You want to seek help early in the process and we encourage you to engage with SBIR programs path with appropriate expertise.

You need time to fill the gaps, to assemble the team, to get access to equipment and other resources which is part of the application and get letters of support. You do want to talk with the customers, experts and investors and commercialization partners - potential commercialization partners - when applying and I'll talk about the letters of support which are expected.

You build a proposal team. Choosing the PI is a very important decision. Consider building the multi-PI team which is very good mechanism for multidisciplinary proposals and is important in cases when PI lacks certain types of expertise.

You must appoint the contact PI and only the contact PI has to be with the small business more than 50% of the time. For the STTR, the PI can be with the research institution.

Remember that reviewers only see the application so you have limited amount of space. Specific aims are limited to one page. Research strategy is six pages in the Phase 1 and 12 pages in the Phase 2. For introductions - for submissions - you can include the introduction.

There are other application components. One component which wouldn't be familiar to the academic grant writers is a Phase 2 commercialization plan which is a critical component of the application.

Letters of support need to be strongly worded and they need to come from all consultants and collaborators paid from the grant, those who provide access to facilities and administrators, key opinion leaders who think highly of the project, customers, partners, investors and suppliers of critical technology.

A good letter of support explains who the writer is, explains the writer's role in the proposals and contains specific support of your institution. You need to know your reviewers and fortunately the CSR publishes the rosters of the past reviews so you are very welcome to visit the CSR website and see the type of the reviewers that your proposal will be reviewed by. More information can be found on our Website and I'll be happy to answer any questions.

Shannon Silkensen:

I just wanted to let you all know that we're experiencing some thunderstorms in Rockville so if you've lost audio, please just hang

up and dial back in to the conference at 1-800-539-9924. The password is cancer centers and also if you have questions that are specific to your personal application, we will answer them via e-mail offline.

So David, somebody wrote in and asked does contract support fast-track mechanisms and if so, what is the maximum amount you budget for these fast-tracked contract applications?

David Beylin: It depends on the contract topic for the contract so in each contract topic, it is specified whether the fast tracks are allowed or not. If they are allowed, you are submitting per instructions two proposals in the same package. The limit for each of the sections for the Phase 1 and the Phase 2 is the same as indicated for the Phase 1/Phase 2 applications.

Shannon Silkensen: If a startup company has applied for a grant topic that wasn't initially funded, is it worthwhile for them to reapply with new data?

David Beylin: Absolutely. Most companies especially those new to the process do not get funded the first time so a resubmission is the norm and if you have new data, it's really worth applying.

Shannon Silkensen: Are the previously awarded SBIR contracts disclosed anywhere?

David Beylin: Yes. Both grants and contracts are - the titles, the names of the investigators and abstracts - are publicly available. You can find all of them through the NIH reporter system.

Shannon Silkensen: Got you. So what efforts are being made to reduce the time from application submission to award?

David Beylin: This is a great question. Unfortunately the key component over the NIH system is the peer review as you all know and it does take a significant amount of time to put together a review and give the reviewers time to look at the proposal so all the efforts to reduce the time from application submission to award are within the peer review system, the center for scientific radiology department of extramural activities.

Shannon Silkensen: So if I've submitted - one of the PIs asked - if they've submitted an application and the NCI was listed as a secondary reviewer or institute, what is the likelihood that the NCI will pick it up and either pay all of it or it'll be co-funded between the NCI and the primary institute?

David Beylin: Well, in this case it's best to be proactive. It's very unlikely that NCI - it does happen but it's very unlikely - that NCI will look at the secondary application and will consider it for funding.

However if you are proactive and you contact the program director listed and this is a well-reviewed proposal that NCI is interested in, there are instances when the proposal may be transferred to NCI or in very many cases because NCI is a fairly competitive institute outside of NCI.

Shannon Silkensen: Got you.

David Beylin: The time to do it is usually after the review.

Shannon Silkensen: So will you recommend applying for NIH SBIR funding if the NIH has not actively solicited the exact topics that they're researching?

David Beylin: Yes, absolutely. The SBIR Omnibus solicitation is the mainstream solicitation at NCI and it encourages applications with investigator-initiated research so most of our funding actually goes to topics which are identified by applicants and not by NCI.

Shannon Silkensen: Great. Can you talk a little bit about how to decide whether to apply via the Omnibus or through a specific funding announcement?

David Beylin: Usually if you are a great fit for the FOA with your technology then funding opportunity is - going after a specific funding opportunity - is preferable. For example for the contract topics, the review is much more focused.

There are many reviewers on the panel with an expertise which very well matches the proposals and there are also reviewers with commercialization expertise in your particular field.

So if you are a better fit - if you are a good fit - to a specific solicitation, specific contract topic, it's generally preferable to apply for that because you will be getting very high-quality review.

Shannon Silkensen: Great, and just one last question which is sort of general. How do SBIR contract applications differ from the SBIR STTR grant application?

David Beylin:

Well, first of all they are on paper. The contract applications are still on paper and the exact format is discussed in the RFP for the contracts as we are in a city, our grant applications are electronic and are submitted through grants.gov. There are numerous formatting differences but overall the philosophy and expectations both for the grants and contracts are fairly similar.

Shannon Silkensen:

Great. Thank you very, very much, David. We're now going to hear from Jim Olson who's both a member of the Fred Hutchinson Cancer Research Center in Seattle as well as the President of Presage Biosciences. You ready, Jim?

Jim Olson:

I am, thank you very much. So in this first slide I list just three points but there's a lot of history behind these three points. When we founded Presage, first of all we had six years of laboratory-based research and for me the key things in starting a company and spinning this out of the Fred Hutchinson Cancer Center was that I really wanted the technology to be proven already so that the risk of failing was lower.

And more importantly I wanted to make sure that I had a really strong business partner that would take that portion of the new company and really make it fly. I have heard the statistics that 90% of new startups that come out of academia fail and I did not want to contribute to that number. I wanted to be one of those that succeeded.

We were incorporated in November of 2008 and the key thing about that particular date is that we incorporated just days before the stock market crashed the first time in 2008 and that becomes important as we talk later about obtaining funding from investors.

We submitted a Phase 1 application to the NCI in December of 2008 and here you can see that this submission was just three weeks after we incorporated the company which I think emphasizes the point that Michael made which is you want to apply early knowing that feedback from the reviewers can help shape the way that you build your company and your message to your investors.

And also because there is a timeframe between the time that you apply and the time that you receive the grant. The next slide shows a picture of one of my patients. I'm a pediatric neuro-oncologist. I take care of kids with cancer. This is a little boy who was visiting my laboratory and the work that Presage does is directly coming from our clinical experience.

As a oncologist it was frustrating to me that each time a patient has a relapse with their cancer, I'm prescribing chemotherapy without having any idea whether their cancer is already resistant to the medicine that I'm prescribing.

If their cancer is resistant to the medicine I'm prescribing, then what I'm prescribing to them is a medicine that will cause severe side effects without providing any benefit and often this is the only opportunity you get so there is an opportunity cost of treating those same kids or adults with cancer drugs that might work.

To address this, I hired two engineers to work in my lab to develop a platform in which we could inject small amounts of chemotherapy directly into different places within a tumor to find out which ones worked and which ones did not work.

The idea would be if you injected a drug directly into the tumor, show that the drug engaged its target and the cancer cells failed to respond to it, then you really wouldn't want to prescribe that drug to a child or an adult with cancer.

I'll show you what that technology looks like in just a couple of minutes. Now interestingly the investors gave us feedback that shaped the company and it turns out that the NCI kind of came to the rescue with that core goal that I just laid out for you.

When we talked about this first with investors, they felt that this clinical application was very high risk but also very high reward and that they were asking how will the FDA work with us on something that is both a device and an in vivo diagnostic application?

They raised the question of could they feel good about investing at that particular time when the stock market had just crashed in a platform that did not yet have human data and they pointed out and this is really what shaped the company that there was nearer-term commercial opportunities if we worked with pharmaceutical companies to use our platform for preclinical diagnostics and preclinical support of adding value to the drugs that are being developed by a pharmaceutical partner.

And this is what I'll show you in a minute and you'll see that the ways that we worked with pharmaceutical companies have not only brought revenues into the company immediately but they also provide a huge amount of support for building the platform in a way that will make us most successful when we go to our human patients.

So let me tell you a little bit about what Presage is today, introduce the technology to you and then come back to how the STTR grant that we received played into this.

Right now we're working with multiple pharmaceutical companies to help them discover more effective drugs and drug combinations. We have already provided data to our partners.

In one case it provided a decision where they decided not to move forward with the drug they were developing and it saved a young company somewhere between \$10 and \$60 million that probably would have caused the end of their company because the drugs that they were working on when they engaged the target failed to cause an effect and it would have been a really poor decision by that company.

We've provided data to another pharmaceutical company that will help them make decisions about which drug combinations to bring into human clinical trials and for that particular company these are compounds that already have human data, have little or no efficacy as a single agent.

But when we found combinations of drugs that worked effectively in human tumors grown in mice, this gives them an opportunity to bring that immediately to human clinical trials and if they receive an FDA approval, that could result in one to \$1.5 billion a year in revenue stream so there's very high value for the drug companies at that level.

The diagnostic device that I just told you about where we will actually do precise microinjections into individual patients is on track

for the first clinical trial studies in 2012. That will be in lymphoma patients.

Presage now has 12 full-time employees. We have \$7 million in funding both through private equity as well as pharmaceutical contracts and we have multiple pharmaceutical partners.

Now this is the basic premise of this which is that most drug discovery takes place on cancer cells that are grown in plastic dishes. They're grown as monolayers. They're grown in the presence of bacteria and we learn a lot from this. It's fast, it's inexpensive but it's often misleading.

Cancer cells do not behave the same way under those conditions that they do in a patient and so the technology that we developed really takes advantage of the microenvironment and helps understand how cancer cells die when they are in the normal environment of paracrine signaling and talking to each other.

This next slide shows a close-up of our technology and what you see is that we've designed an array of porous needles. Each of these needles is engineered to be like a little miniature soaker hose.

The original idea was that each could be a substitute for a capillary and arterial that would deliver a different chemotherapy to different parts of the tumor so that we could see when a tumor received a chemotherapy, did it engage its target and if so what was the response.

Typically what we do is insert these porous needle arrays into a mouse that's carrying a human tumor. We insert it into the tumor. We inject the drug, a different drug through each needle.

We co-inject a marker, in this case a near-infrared dye that tells us exactly where the drug was injected into the tumor. We leave that in place for a few minutes, remove the needles, and let the mice walk around for about three days while the drugs take effect.

We then sacrifice the mouse, fix the tissue, slice it crossways to the needle which gives us the world's only platform for doing a multiplex analysis in vivo in human cancer.

Here's an example that shows another view of the device and it shows a cartoon of the porous needle and to the right of that you see slices through the thickness of a tumor and this is really important.

This is a key component of our technology because as you know cancers are heterogeneous and if we just took a regular needle and squirted a drug into a tumor, if we found that cancer cells were dead near that injection site, we wouldn't know if they were dead before or after we injected the drug.

In this case each needle creates a unique geometric shape going through the tumor and that unique geometric shape offers the opportunity to find out whether the drug is hitting target and if so whether the cancer cells are responding appropriately at many levels to the tumor.

Because we can get up to 400 slices of tissue through the tumor along each needle assay, we can actually look at many endpoints and see whether biomarkers are confirming the change that the target has been engaged by the drug.

There are three areas that we work with with pharmaceutical companies. First is that because we use small amounts of the drug, we can actually do in vivo studies with premedicinal-chemistry quantities of drugs or compounds so we can not only validate targets but we can also evaluate lead compounds before companies spend millions of dollars on medicinal chemistry.

The second area that we work on is drug combinations and identification and I'll show you some data from that in just a minute, the bottom line being that we can identify combinations of drugs that work more effectively than individual drugs and we can also find the best group of patients for a company to bring their drugs into clinical trials.

And the third is clinical drug selection and this is the area that I told you about at the beginning and this is the area that's funded specifically by NCI through our STTR grant and the question here is can we help patients identify which drugs they should or should not go on in their clinical trials and perhaps whether there are combinations of drugs that would work better for that patient than individual agents.

Here's an example of some of the data that we've presented to one of our pharmaceutical partners. The data's been redacted so I won't be showing you any drug names but the point here is that we can inject

Drug A at a concentration that doesn't cause any effect on its own introduced to Drug B at a concentration that doesn't cause any effect on its own.

And then introduced those same two combinations together at the same concentration through a third needle and you see here that when we do this in a tumor that has a particular molecular driver that we believe this combination could potential be more effective than either drug alone that where we injected Drug A, the cancer cells did not respond to the drug at the concentration injected.

And likewise where we injected Drug B, the cancer cells did not respond to the drug at the concentration injected. Where we injected the two drugs together, you see that the cancer cells responded dramatically and died.

We see the same response with this combination of drugs regardless of whether the combination is injected into the center of the tumor or around the periphery so we know that it's not simply that the center of the tumor is more prone to necrosis.

Furthermore if we inject this combination of drugs into another tumor that has different molecular drivers - in other words it's driven by other - we see no activity which tells us that this combination is specific for the type of cancer that we're trying to address.

Here you see another close-up of a drug combination study and in this particular case we're showing you data in which the cells that are dying are coded in red and what you see is that this combination of

drugs is specifically killing the cancer cells within the islands of cancer cells in the enlarged portion on the right.

And you see the stroma, which is the normal cells that are not cancerous, is spared by this. This tells us two things; one is that the drug is cancer cell-specific and more importantly that that it's not simply a toxic combination of drugs and that it has specificity for the cells that have the particular molecular driver.

So with this type of data, our partners can go directly to either more advanced preclinical studies in a larger cohort of mice and remember that this is the bottleneck in most pharmaceutical companies where it takes tens of millions of dollars and many years to go through multiple combination studies.

We can do that in a year or two and help prioritize which compounds should be researched into in vivo pharmacology studies. In some cases such as the ones I've shown you, these drugs and mature and decisions could be made to go into patients rather quickly.

And likewise in several conversations that we've had with thought leaders in the comprehensive cancer center network, they would like to use this approach specifically on their patients where they would inject Drug A through one needle, Drug B through a second needle and the combination through a third needle.

And if they find that the combination than either drug alone, it would make a go-forward decision for that patient whether it be in a clinical trial or in an individualized oncology setting so now I'll move on to our STTR history.

We initially applied for a Phase 1 application in November of - actually December of 2008 - and we wanted to apply for Phase 1 because our understanding was it's a bit easier to get these on the fast-track agent.

It was a straightforward application to write and what we got back in the reviews was that there were really no concerns about the science that we proposed but there were a lot of questions about the business side of it.

We had those answers. We actually had most of them at the time that we submitted the grant but because of the six-page limit, you're only able to put in a paragraph or two about your business plan.

And so because most of the questions were about the business side of it and the fast-track application - or the Phase 2 applications - allow you to submit up to a 12-page business plan, we resubmitted as a fast-track application in April of 2009.

That was awarded and we received the Phase 1 award in June of 2010 and Phase 2 award in July of 2011 having completed all the milestones of Phase 1. Now if you look at these dates you'll see that from the time of initial submission with one rejection which as David pointed out fits in the norm that it was from the end of 2008 until the middle of 2010 before the funds came through.

So it's really important to keep this in mind and to get your SBIR and STTR applications in early so that you have time to do your revisions and get the awards later. Now there are some things that came

through that were really valuable for us even in going through the review process.

So when we submitted the Phase 1 application and it came back with glowing reviews from this panel of experts not only in oncology but also the panel includes people who are in the pharmaceutical industry, in biotechnology and people who have a lot of experience in the venture area, we were able to share with our investors that this panel of 20-25 experts from the science and business side had glowing things to say about our technology.

And this was really important because some of our individual investors felt that they could not do that level of diligence and so they used this as a surrogate for some of the diligence that a big BC might do.

And we had decided by this point that we were preferring to fund our company through individuals and ultimately that's how we funded this company was through a few dozen investors who provided the venture - the capital - that we needed.

Now importantly I want to point out two other interactions that we've had with the NCI SBIR program. The first was that we were invited to participate in the NCI investor forum in November of 2010. First this was an incredible honor. There are I believe over 400 companies that are supported through the SBIR program.

In Q1 a very small number that were selected - I think there were somewhere in the range of 14 companies that were selected - to present was a great honor. Importantly the audience was filled with

venture folks, people from the pharmaceutical industry, from biotechnology and at that time we were already funded.

We were not looking for new investment and so we focused on partnering meetings while we were there and as it turns out those partnering meetings have been very beneficial.

And the representatives from two of the companies that we met there introduced us to other members of their companies and we're now in late-stage negotiations for multi-year alliances that will dwarf anything that we've done in the past and which would allow us to really provide value to these pharmaceutical companies as they develop new drugs.

The second thing that I'd like to point out is the regulatory assistance program. This is a new program that was not mentioned in the early part of the program and the point here is that the NCI in a competitive fashion allowed us to submit applications for receiving assistance on the regulatory side and provides 30 hours of regulatory assistance from one of the nation's leading regulatory groups.

And for us this allowed us to not only come up with a regulatory strategy of how do we go to the FDA but also to put that into a Gantt chart that allows to have very specific timeline. It's been extremely helpful to our company.

So a couple of last things that I'll mention before we go to the questions, one is I really appreciate the fact that this conference is being sponsored by the cancer centers.

Fortunately NCI, it was cancer center pilot grants that helped us get started with the technology. The engineers that I mentioned, the post-doctoral fellowships were funded through NCI comprehensive cancer center pilot funds. Also I think that through the NCI both programs we've had an opportunity to meet others in the cancer drug discovery field.

And one of the things that we've been hearing from universities around the country is that they're having a hard time licensing their cancer drugs out to the pharmaceutical industry and they've asked us to potentially serve as an intermediary where we could get in vivo data on their premed chem or later-stage oncology drugs and then partner with the pharmaceutical industry to license.

This provides a win-win for the academic institutions as well as for the pharmaceutical companies because if we go to a drug company and say look, we've looked at about 40 or 50 drugs and these are the three or four that you should care about, that provides a real incentive for an effective licensing agreement.

Furthermore by working with a number of academic institutions, we're able to treat the academic groups with their permission and cooperation as a larger pipeline that allows us to identify combinations that add value that would be not found elsewhere so our primary focus remains on our partnerships with the pharmaceutical companies.

We're looking at mechanisms by which we can work with an academic consortium and most importantly because the NCI really did come through and save the day on the patient applications, we're

going to be able to go into human clinical trials and bring this technology into patients to help identify the best drugs for individual patients with cancer with the first trial beginning in about a year. I'll be happy to take questions.

Shannon Silkensen: Great. Thank you very much, Jim. We've received a couple of questions online. One of the things that people were wondering about is do many of your employees also have academic appointments at cancer centers or are they employed fully by Presage?

Jim Olson: Right now almost all of our employees are fully employed by Presage. There was a period of time when the company was first starting that some of the employees had a part-time position at my laboratory and a part-time position at Presage. We've put in the appropriate conflict management plan at both places to ensure there was no problem with using laboratory resources.

Furthermore Presage has been able to provide sponsored research agreements with my lab and with the Hutchinson Center so that those things that would be important to do but would otherwise create huge capital needs for a small company can still be done through our cancer center under a sponsored research agreement in which Presage paid not only for the research but the indirect as well.

Shannon Silkensen: So a really nice relationship for you, huh?

Jim Olson: Yes.

Shannon Silkensen: Can you speak a little bit about trial or data ownership, when you either work with a large pharmaceutical company or again with an academic institution, how is this sort of worked out ahead of time?

Jim Olson: Yes. It's certainly different for both and obviously this isn't the right forum to go into details on that. The bottom line is that when we work with pharmaceutical industries, we really focus on having long-term royalties and such on those things in which we co-invent and I think I'd prefer not to say more about that at this point.

With the academic institutions again we are looking for a mechanism by which the academic institutions would get at least as much if not more out of the deal as they would if they were doing this alone.

And we're looking at ways to make sure that it's as simple as possible for the pharmaceutical companies to license it from the academic institutions knowing that sometimes the technology transfer offices can be a bit slow and sometimes a bit of a barrier to commercialization.

So in the models that we've been looking at, it's very easy for academic investigators and institutions to participate with us and it's very easy for the pharmaceutical industry to license these drugs without a protracted negotiation.

Shannon Silkensen: That's great. One of the things you also spoke about was sharing your data or your progress with your investors. Can you talk a little bit about the frequency of those meetings and how you decided what would be shared kind of when?

Jim Olson:

Yeah, that's a good point. There's a lot of things that you learn as a company grows and initially we had setup a schedule where we communicated with our investors every quarter.

And one of the things that we learned over time and which, you know, which is really a problem in a lot of large companies particularly public companies is that providing updates on a regular schedule requires that sometimes you're providing an update when you have an incomplete story and maybe you would have a complete story a few weeks later.

And so in discussions with our investors, we now keep them very frequently updated but we do it when there's something to announce rather than on a time-based schedule, importantly because our company is funded by a relatively small number of individual investors, we really think of it - or investors - we think of it as a family.

And we have our in-person meetings often at my home. We have some people that fly-in from other states for those meetings and importantly our investors bring a lot more to the table than funding, those who are engineers have provided guidance and advice on where we can get the right kind of consultation that we require, those who have a lot of experience.

One of our board members was the first president of Microsoft. He's been able to help us be connected with information folks that help us protect our data so that we don't have any leaks from one company to another.

And likewise one of our other board members is the former head of oncology at Bristol-Myers Squibb so he's been able to provide both context in the pharmaceutical industry as well as guidance on how to be successful in building a biotech company since he did that three times before going to Bristol-Myers Squibb.

So our investors are really part of our family and they're stopping by the company on a frequent basis and we keep them very closely appraised of what we're doing.

Shannon Silkensen: Great. We have one last question, Jim, just give me a second. Did you have to fully relinquish your position at the university to start Presage?

Jim Olson: Actually, I fully retained my position at the university so currently my time is spent 90% in academia and 10% in the commercial side which is the amount that's allowable through the Fred Hutchinson Cancer Center where I'm employed.

And so we recruited Rich Klinghoffer who was formerly with Merck to be the head of biology for Presage, Caitlin Cameron is our CEO and they really run the company. I provide scientific guidance as well as strategy conversations and I meet with the pharmaceutical industry partners to help shape the type of alliances and the scientific work that we'll be doing.

But I run a 20-person research lab and I also see patients at the Seattle Children's Hospital and I was not required to relinquish anything in starting-up Presage.

Shannon Silkensen: That's great. It sounds like you have a very busy schedule. At this time we'd like to open the floor up for questions for all of our presenters, for Jim, David and Michael and so thank you Jim for showing us how you've used SBIR dollars to the best. This is a really, really great example and we're looking forward to seeing great results from Presage in the future.

One of our participants wrote in and asked a question I think that's going to be directed to Michael and this has to do with if at the time of awarding of funding if the PI is no longer able to dedicate 51% of his time to the research project, can the PI be changed of the grant; can the PI of the grant be changed?

Michael Weinstein: Yeah, so one thing I want to clarify is that the requirement is that the PI spend more than 50% of their time with the company but they don't actually have to have over 50% of their time on the particular project and so that's one key important point.

Again the minimum amount of time a PI can spend on a particular project is 10% of their time but, you know, so there's a range there again beginning at 10%.

The other thing if a change does need to be made from the application itself, the best thing to do is to talk with your program director responsible for your project, the person who was assigned and just you would need NCI's approval for that change to be made and we would be looking for someone who has comparable expertise to the original PI for us to approve something like that.

Shannon Silkensen: Thank you, Michael. Our next question is for David. For the specific topics in your presentation, how best should the applicant engage with the program director?

David Beylin: So the answer differs for grants and for contracts. For grants you can really engage with the program. You can - one of the ways to find the right person - is to e-mail one of us and we will triage you to the program director with the most interest in the area you want to propose in.

For the contract, we cannot provide you with any specific guidance after the RFP is published on your particular project so if you have specific questions related to your project, you are encourage to contact the NCI person at the Office of Acquisitions who is listed in the Request for Proposal.

Shannon Silkensen: Thank you, David. Somebody else asked Michael can a company submit an application to the Omnibus proposal early to get feedback from the NCI and resubmit? I guess what they're trying to figure out is how much input can they get from the NCI before the actual application goes through?

Michael Weinstein: Yeah, so if you're working on a grant application and you'd like to get some input from NCI ahead of time before you actually submit it, you're welcome to contact us.

And the way we're setup is we are - our program directors - are responsible for different aspects of the portfolio so, you know, it's probably setup a telecom to discuss your intended application and to

provide you some feedback. That's probably the best way to do it as opposed to, you know, submitting your full application.

Shannon Silkensen: Got you. Another sort of process question that we've received has to do with the contracting timeline so sort of roughly how long does it take for the contract mechanisms from the NCI contract to go from submission and then the pause between submission and review, again there's a pause between review and selection of funding to the contract submitter actually getting the money?

Michael Weinstein: So it's typically between when the submission date of November which for the contracts they are due November the 7th this year so typically we will or actually the contracting officer would contact companies that have submitted and gone through peer review, have been scored.

They will probably find out in the June timeframe if the NCI would like to initiate negotiations with them over the contract and then the negotiation process would typically take a couple of months to actually get it in place so awards would typically be made - for proposals received in November - awards would typically be made in say August or September.

Shannon Silkensen: Great. Thank you, Michael. I think at this point we've answered most of the questions that we've received from the general audience so I wanted to say thanks again to our speakers, to Jim, Michael and David and also thanks to all you all for being on the call.

If you have any questions about the NCI SBIR program that weren't answered today, please just send a quick e-mail message to ncisbir@mail.nih.gov. Thanks so much. Bye bye.

END