SPARC FULL PROPOSAL

**INSTRUCTIONS:**

This document is provides guidance on content for your full project proposal to SPARC. A successful proposal to SPARC will be referenced in an executed collaboration agreement under the SPARC-WUSTL Master Services Agreement for your technology.

The goal of this document is to demonstrate the *ideal* level of detail and *format* of content that outlines your project for SPARC. Every single item in this guidance document does not have to be incorporated into your specific project proposal, some items may not be applicable to your project based on technology type or stage.

The best proposals utilize feedback from the Center for Drug Discovery and the LEAP Development team to hone content & detail. Send proposal drafts to Tom Krenning (Assistant Director of LEAP & Research Innovation, tomkrenning@wustl.edu) and to facilitate feedback.

Full Proposal Outline:

* **SECTION 1: MARKET & NEED - 1 page**
	+ What is the unmet need your project addresses? What is the competition?
* **SECTION 2: THE TARGET PRODUCT PROFILE - 1 page**
	+ Describe the advantages over the standard of care
* **SECTION 3: CLINICAL TRIAL CONSIDERATIONS – 1 page**
	+ Outline your initial clinical trial
* **SECTION 4: PROJECT STAGE, GOALS, & PLAN**
	+ **CURRENT PROJECT STAGE – 2 pages**
		- Description of the current status of data to demonstrate proof of concept.
	+ **DEVELOPMENT MILESTONES – 1 page**
		- What are the aims of the collaboration?
	+ **DETAILED DEVELOPMENT PLAN – 3-5 pages (w/o tables)**
		- What activity is planned to achieve the **DEVELOPMENT MILESTONES**?
		- Who will perform this work and how will it be funded?

Total pages= 11 maximum w/o tables

[PI Name] FULL PROPOSAL

**Project Title:** *(Product description) for (indication)*

**Lead Investigator:** *Full name, official university title*

**Lead Investigator e-mail:**

**Executive Summary**: *Provide a 200-250 word description of the project. Outline the mechanistic basis, the current stage of development of the proposed therapy, the advantages over the standard of care, and the development activities needed to identify and validate a clinical candidate based on your knowledge.*

**Key Project Leadership**: *Provide a brief description of the technical and operational management team’s qualifications. Be specific about what kind of experience and for how long. This should be a maximum of a couple sentences per person.*

**SECTION 1:**

**THE MARKET & NEED – 1 PAGE**

**Unmet Need/Target Market:** *This section should address every question and sub-question below to the best of your knowledge. Projects with accessible initial markets and follow-on markets tend to be attractive.*

1. *For your initial “go-to market” indication: To the best of your knowledge, what is your proposed FDA/EMA indication statement and patient population to be treated (eg., 2nd line treatment of mild-moderate acne in 12-25 year olds)? Select the indication with the largest unmet need, simplest clinical trial & lowest regulatory burden based on your current understanding.*
	1. *What is the general prevalence of this patient population in the U.S. & globally? What data supports this estimate?*
	2. *What are the existing therapies, including therapies in clinical trials, for the proposed indication or for the same biological pathway? Make a comprehensive list of the relevant drugs in your therapeutic space in a table of the format below:*

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| --- | --- | --- | --- |
| *Compound* | *Company* | *Mech. Of Action* | *Development Stage* |
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* 1. *Briefly, what is the supporting rationale for your proposed advantage over existing therapies? You will answer more comprehensively in Section 2.*
1. *For potential follow-on indication(s): To the best of your knowledge, what are your proposed FDA/EMA indication statement(s) and patient population(s) to be treated? Select the indication with the largest unmet need, simplest clinical trial & lowest regulatory burden based on your current understanding.*
	1. *What is the general prevalence of this patient population in the U.S. & globally? What data supports this estimate?*
	2. *What are the existing therapies, including therapies in clinical trials, for the proposed indication or for the same biological pathway? Make a comprehensive list of the relevant drugs in your therapeutic space in a table of the format below:*

|  |  |  |  |
| --- | --- | --- | --- |
| *Compound* | *Company* | *Mech. Of Action* | *Development Stage* |
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* 1. *Briefly, what is the supporting rationale for your proposed advantage over existing therapies? You will answer more comprehensively in Section 2.*

**SECTION 2:**

**THE TARGET PRODUCT PROFILE – 1 PAGE**

**Product Summary**: *Describe the advantages of your asset* ***once developed*** *that distinguish it from the standard of care (SOC) to the best of your knowledge. Specifically, describe in writing* ***advantages over SOC*** *in the following areas (as applicable):*

* *The mechanism of action and how it modulates the disease state for patients falling under your proposed FDA/EMA indication statement as compared to existing or investigational therapies. Be specific in your description, but keep recitations of data to a minimum needed. You’ll describe that further in* **SECTION 4***.*
* *Other strategic advantages of your product over existing or investigational therapies, e.g., route of administration, desired pharmacokinetics, stability / storage conditions, treatment setting, formulation maximizations, manufacturing cost, etc.*

*Then fill out the below* **Target Product Profile** *table to the best of your current knowledge. This is an exercise that every serious clinical asset will go through at some point in its development.*

* + *The “Ideal Target/Claim” describes the specific characteristics your product must have to access the* **full** *patient population or market. If you are going* **maximize** *your value proposition to patients, doctors, insurance companies, hospitals and your potential licensee or acquirer, what characteristics must your product have to succeed in the clinic to its* **fullest****extent***?*
	+ *The “Minimum Acceptable Target/Claim” describes the specific characteristics your product MUST have to achieve the* **minimum** *level of advantages over the standard of care to address a significant unmet need in the clinic. What is the* **lowest threshold** *you have to hit to be successful?*

*The “Req. Evidence” refers to the 1) clinical endpoints to be evaluated to prove your advantages in the clinic and 2) animal data needed to demonstrate that product is defined by said characteristics. Indicate whether or not this animal data has already been acquired.*

| **Target Product Profile to Differentiate from Standard of Care** |
| --- |
| **Ideal Target / Claim** | **Min. Acceptable Target/Claim** | **Required Evidence** |
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***FDA generated example Target Product Profiles (TPPs) found*** [***HERE***](https://www.ninds.nih.gov/Funding/Apply-Funding/Application-Support-Library/CREATE-Bio-Example-Target-Product-Profile-TPP)***.***

***Full FDA Guidance Document on Target Product Profiles found*** [***HERE***](https://www.fda.gov/media/72566/download)***.***

**SECTION 3:**

**CLINICAL TRIAL CONSIDERATIONS – 1 PAGE**

*This section contains your assessment of the clinical & regulatory path with the aim of demonstrating to SPARC that the activities are feasible. Based on your current knowledge, what strategies can you take to ensure that your eventual clinical trial will be of reasonable size (i.e. not tens of thousands of patients over 10+ years)?*

*Describe the first potential clinical study to demonstrate proof of mechanism and addressing the points below:*

1. *Patient stratification/selection for the study (i.e. molecular signature, SNP, genetic deficiency etc.) This is important to ensure that patients are selected based on their likelihood to respond.*
2. *Clinical study endpoints that would allow for testing mechanism in patients and speak to the proposed FDA/EMA indication statement.*
	1. *Will your endpoints allow for clinical differentiation from other therapies?*
	2. *This is important to accelerate statistical differentiation from benchmark therapies so that less patients need to be enrolled and study cost can be minimized.*
3. *Are there longitudinal monitoring / follow-ups required for this patient population? This activity will increase overall study cost.*

*Address critical efficacy- based Phase II/III Trial Considerations:*

1. *In your target patient population, what would you expect your primary (and secondary) clinical endpoint(s) to be in a pivotal study? You may not have full clarity of this at this stage, but speak to what you know.*
2. *In your intended target population, are there any factors that might preclude full responses to treatment?*

**SECTION 4: PROJECT STAGE, GOALS, & PLAN**

*The purpose of this section is to go deeper into the data & current status of the project and outline a detailed plan with milestones for development.*

**CURRENT PROJECT STAGE – 2 PAGES**

*What specific data do you currently have available to support that your product will function as required and that your development plan is reasonable? Where do things currently stand?*

* *What are the main points in the story of your mechanism of action? Which of these are most important to differentiate your proposed therapy from the standard of care?*
	+ *Describe the genetic evidence supporting the mechanism of action for your therapy and the advantages over standard of care.*
	+ *Describe the pharmacological evidence supporting the mechanism of action for your therapy and the advantages over standard of care. Specifically, address the data you have generated to support the below. You may not have much data to speak to this, but describe what you have now. You’ll describe what you need to generate in the following sections*
		- *Relationship between pharmacokinetics-pharmacodynamics*
		- *Lack of toxicity & acceptable safety margin*
		- *Favorable metabolism and excretion*
		- *Biocompatibility & immunogenicity*

**Intellectual Property – 1 Paragraph**

* *What intellectual property do you currently have in hand & what does it cover? Work with your OTM representative on this.*

**DEVELOPMENT MILESTONES, DECISION POINTS, & SUCCESS MILESTONE**

**– 3-5 PAGES w/o tables**

*This section is a narrative describing the relationship between the desired properties of your new product (outlined in your* **Target Product Profile***) and the steps needed to demonstrate those key properties with experimental data. If these critical properties can be demonstrated, then the project is worthy of continuing. Attainment of* **Development Milestones***is a product of the specific activities needed to demonstrate the properties outlined in the***Target Product Profile***.* **Decision Points***prospectively quantified data thresholds based on the data generated by the specific activities which support a* **Development Milestone***. This allows for a clear assessment of whether the project is hitting* **Development Milestones** *at the expected pace.*

**Development Milestones** *are similar to the “Specific Aims” in a grant application except that there is a greater emphasis on this* ***prospective*** *&* ***quantitative*** *definition of**success which denotes a* **Decision Point*.*** *Setting of* **DECISION POINTS** *in scientifically appropriate places is important for this proposal to be attractive to SPARC.*

*The clear end goal for this collaboration is the* **SUCCESS MILESTONE.** *This must be attained by the end of the relationship. Generically, this is:*

**SUCCESS MILESTONE: *Identification & validation of a clinical therapeutic candidate which demonstrates an advantage over the standard of care.***

*Put the above* **SUCCESS MILESTONE** *for the collaboration into your own words for your project (see table below).*

*To draft your go/no go* **Development Milestones***, begin with the end in mind:*

* *Start with your* **SUCCESS MILESTONE** *and outline the activities required to get there. Think about the full set of data needed to demonstrate validation of your asset as a clinical candidate having significant advantages over the standard of care.*
* *What is the plan of attack to generate this data? What experiments are dependent on one another? What is the sequence of activities?*
* *What data is most important to obtain?*
* *In the above, is every required element of your* **TARGET PRODUCT PROFILE (TPP)** *captured?*
* *What data to validate your* **TPP** *is missing from the* **CURRENT PROJECT STAGE** *section above?*
* *The completion of the specific activities needed to generate data to validate your* **TPP** *are the* **DEVELOPMENT MILESTONE(S)** *and the data need to successfully meet these are the go/no go* **Decision Points.**

*Draft your* **Development Milestones** *and* **Success Milestone** *in the tables below. You can group the types of milestone by category as it makes sense for your project. For example: “Translational Biology” (i.e. developing models and exploring biology), “Drug Discovery & Development (i.e. process of identifying promising interventions),” or “Pharmacology and Safety Assessments” (i.e. evaluating the most promising interventions).*

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| **SUCCESS MILESTONE:** | **IDENTIFICATION & VALIDATION OF A CLINICAL THERAPEUTIC CANDIDATE WHICH DEMONSTRATES ADVANTAGE OVER STANDARD OF CARE.” 🡨 Put this in your own language for your project.** |

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| **DEVELOPMENT MILESTONES** **/ DECISION POINTS:** | **[Type of Activity]**1. **KEY GO/NO-GO DATA THRESHOLD TO BE ACHIEVED – MONTH/YEAR**
	1. **Specific activity**
	2. **Specific activity**
	3. **Decision Point 1 (DP1)**
2. **KEY GO/NO-GO DATA THRESHOLD TO BE ACHIEVED – MONTH/YEAR**
	1. **Specific activity**
	2. **Specific activity**
	3. **Decision Point 2 (DP2)**

**[Type of Activity]**1. **KEY GO/NO-GO DATA THRESHOLD TO BE ACHIEVED – MONTH/YEAR**
	1. **Specific activity**
	2. **Specific activity**
	3. **Decision Point 3 (DP3)**
2. **[add more as needed]**
	1. **Specific activity**
	2. **Specific activity**
	3. **Decision Point 4 (DP4)**
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**DETAILED DEVELOPMENT PLAN**

*Overall the* **Detailed Development Plan** *consists of three things:*

1. **Written Description of Development****Milestones**
	1. *Written and tabular depiction of specific activities to achieve the Development Milestone*
2. **Development Milestone Flowchart or GANTT Chart**
	1. *Graphic depiction of the* **Development Milestone** *dependencies and* **Decision Points**
3. **Use of Funds Table**
	1. *Budget for each year outlining the experiments, reagents needed, funds required, and quantified data readouts.*
4. **Written Description of Development****Milestones**

*In this section, the subheadings are each of the* **Development Milestone(s)** *and below each is provided further explanation of the main specific activities by describing the items in the list below that are needed to achieve the milestone. The more detail, the better, but don’t too caught up in this description. We can work on these activities together with SPARC.*

* *Experiments & assays*
* *Needed reagents: just those that are not easily commercially available*
* *Expertise needed and source of expertise (i.e. SPARC, specific WUSTL collaborator, member of PI’s lab)*
* *Location of Work performed;*
* *Schematics that describe the rationale for prioritization of various hit and lead compounds; and MOST IMPORTANTLY*
* ***Quantification (not qualification) of the data acquired from experiments to denote the go/no go Decision Point for the Development Milestone.***

*Also, in this section is a tabulated depiction of these written specific activities for each* ***Development Milestone****. See template below. This goes under each* **Written Description of Development****Milestone.**

|  |  |  |
| --- | --- | --- |
| **Assay / Experiment / Activity (Special reagents Needed)** | **Group Performing Work** | **Specific Data Readouts** |
| [Description of specific activities required under this tranche – EACH EXPERIMENT IS ITS OWN LINE, add as many lines as needed] – (Describe any particular needs for reagents to complete the activity in parentheses)This is NOT: “In vitro testing” or “Demonstrate manufacturability”This IS: “Testing Patency and Efficacy in a diabetic pig model on 8 pigs” | [PI last name] Lab or Acronym | [specific success criterion for the deliverable which is clearly “go/no-go”]This is NOT: “Favorable Pharmacokinetics” OR This IS: * “Demonstration of a 2-4 hour half life and measurable biomarker
* “Reproducibility of survival outcomes within 15%”
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*Some additional guidance on content:*

* *What experiment or activities, if unfavorable, would kill the chance of success of the project? These is the most important activity to engage in to de-risk the project.*
* *Logistical bottlenecks, like identification of hits & prioritization of lead compounds, often are appropriate* **Decision Points***.*
* *Proposals denoting* **Decision Points** *with* ***quantitative success criterion*** *which allow for* ***binary go/no-go decisions*** *are ideal.*
1. **Development Milestone Flowchart or GANTT Chart**

*In this section the milestones and go/no-go criterion and the relationships between each are graphically depicted. See an example of this Scheme* [*here*](https://wustl.box.com/s/q117zebx7199vjf5kea1ola4sp2i2gdf)*.*

1. **Use of Funds Table**

*In this section, the proposed Budget and timeline for each year are depicted in table format. See the template and example Use of Funds Tables below. Include all the experiments, activities, to be completed in one year of the collaboration.*

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| **USE OF FUNDS TABLE****SPARC COLLABORATION – YEAR 1** |
| **Fund Source: SPARC**  |
| **Associated Development Milestone Number** | **Assay / Experiment / Activity (Reagents Needed)** | **Funds required / Group Performing Work** | **Specific Data Readouts** | **Delivery by** |
| [Input the number of the of the Development Milestone that the assay or experiment falls under.] | [Description of specific activities required under this tranche – EACH EXPERIMENT IS ITS OWN LINE, add as many lines as needed] – (Describe any particular needs for reagents to complete the activity in parentheses)This is NOT: “In vitro testing” or “Demonstrate manufacturability”This IS: “Evaluating efficacy in a diabetic pig model, n=8” | [$] – [PI last name] Lab, Group Acronym, or Company (e.g. SPARC in-kind) | This is NOT: “Favorable Pharmacokinetics” OR “Confirmation of mechanism”This IS: * “Demonstration of a 2-4 hour half life”
* “Positive correlation of target occupancy & plasma levels with desired phenotypic outcome in dose response”
* “A safety margin of 40% minimally efficacious dose”
* “Reproducibility of survival outcomes within 15%”
 | [Month Year] |
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| ***Sub-total SPARC funds*** | **Max Direct ~$160,000** |  |
| **Fund Source: non-SPARC** |
| **Fund Source** | **General Aims** | **Funds Available** | **Associated Development Milestone Number / How does this help acheive Development Milestone(s)?** |
| [Granting Agency or other source] | [Description of applicable aims] | [Total funds available / Funds in-Hand or not] | [#] - [How does this help achieve Development Milestone?] |
|  |  |  |  |
|  |  |  |  |
| ***Sub-total Non-SPARC funds*** | $X |  |

**EXAMPLE DEVELOPMENT PLAN:**

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| **EXAMPLE USE OF FUNDS TABLE****SPARC COLLABORATION – YEAR 1** |
| **Fund Source: SPARC** |
| **Tranche # / Pre-Requisite** | **Specific activity** | **Funds required** | **Deliverable & Success Criterion** | **Delivery by** |
| **Tranche 1a / no pre-requisite** | Single Drug Dose Response in ABC model with Drug 1, Drug 2, Drug 3, Drug 4 | $25,000 | At least two drugs which show 15% reduction in liver ABC accumulation at non-toxic doses | March 2019 |
| **Tranche 1b / no pre-requisite** | Regulatory Analysis & Commercialization strategy for re-purposing pathway | SPARC in-kind | Identification of a viable regulatory & commercial strategy leveraging IP to navigate clinical trials | March 2019 |
| **Tranche 2 / pre-requisite:** success in Tranche 1a+b and Quotes from CRO for PK | Drug pair testing of ideal concentrations in ABC model to assess synergy (Drug 1 and Drug 2, Drug 1 and Drug 2, Drug 3 and Drug 4) | $25,000 | At least one drug combination with a combination index of <1.0 via isobologram analysis and lack of toxicity | July 2019 |
| **Tranche 4 / pre-requisite:** success in Tranche 2 + 3 | Studies to address toxicity, relationship of PK-PD, and further validate mechanism (Note: In your proposal these studies should all be broken out into separate lines) | $100,000 | [Success criterion for each of the proposed studies] | March 2020 |
| ***Sub-total SPARC funds Year 1*** | $150,000 |  |
| **Fund Source: non-SPARC** |
| **Fund Source** | **General Aims** | **Funds Available** | **Why is this applicable to your Key Development Milestone?** |
| NIH R21 | Investigation of novel pathogenic mechanisms in the ABC model | $2M | Personnel funded under this grant can be utilized as this activity dovetails with aims |
| [Granting Agency or other source] | [Description of applicable aims] | [Total funds available] | [How does this help achieve Development Goal?] |
| ***Sub-total Non-LEAP funds*** | $X |  |

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| **Post-Year One Funds Needed** |
| **Funding Source** | **Activity** | **Funds required** | **Pre-Requisite** |
| R01 | Pharmacological elucidation of mechanism [Note: this should be more specific] | 3M / 5y | pre-requisite: completion of LEAP Tranche 2 |
| SPARC | Continued Non-GLP PK-PD & non-GLP Toxicology for IND | $200,000 | pre-requisite: completion of LEAP Tranche 3 |
| SPARC, in-kind  | IND-enabling Toxicology, IND drafting and filing, Phase 1 clinical trial | $5M | pre-requisite: favorable non-GLP pharmacology, pharmacokinetics, and toxicology data from SBIR |
| SPARC, in-kind | Phase II clinical trial | $15M | pre-requisite: favorable Phase I results |
| ***Sub-total Post-Year One funds:*** | **$25.2M** |  |