MSU-Molecular Discovery Group Pilot Grant Application

E-mail complete application as PDF to Joseph Nichols DDProgram@list.msu.edu

Application Due Date: Friday, October 15, 2021 at 5:00 PM

Title of Project:

PI Name:

MSU Phone number:

E-mail:

Department:

Co-investigators and departments:

Area of application (check all that apply):

☐ Human Health ☐ Animal Health ☐ Plant Sciences/Agriculture ☐ Other (specify)

Target Product Profile (TPP) (check one, *see attached forms*)

☐ Therapeutics (TTP template 1) ☐ Agricultural (TTP template 2) ☐ Technology/Diagnostics (TTP template 3)

or ☐ Basic Research

1. Abstract (200-word limit)

2. Scientific background and significance. If the project is successful, describe how the technology will be used and what its impact will be. (Limit 1 page)

3. Target product profile (TPP) - Therapeutics (Template 1), Agricultural (Template 2), or Technology/Diagnostics (Template 3) ***Fill out appropriate attached form.***

If a commercial application is envisioned, mark above which area is considered and fill out appropriate attached form. If not, explain how this work will support extramural funding for this program.

4. Describe key work to be completed including time-line, decision-matrix and feasibility relative to key milestones (i.e. short-term laboratory objectives). Explain potential problems/liabilities and how they can be mitigated? Describe how this study fits into a longer-range commercialization plan. (Limit 2 pages)

5. Plan for future funding or commercialization based on work outcome. Identify next round of funding and what data is required. (Limit 1 page)

6. Key literature and citations

7. Budget for proposed work. Up to 10% of the award can be used for project work outside the core labs.

- No funds may be used to support salary
- Funds must be spent within 12 months of award date. Reviews of progress will be provided at mid-term quarter by the PI and core leaders.
- Proposals ***must*** include an attached quote directly from the core(s) for the proposed project. Please consult the staff of each core for availability (see below).

Budget Summary

Item	Cost
ADDRC - Services	
ADDRC - Reagents/Supplies	
MCC - Chemist labor	
MCC - Reagents/Supplies	
In vivo Facility - Services	
In vivo Facility - Reagents/Supplies	
PI Lab Reagents/Supplies (10% or less)	
Total	

8. Biosketch of PI and co-PIs (2-page limit) to be sent with grant application as additional files (not required from core personal).

9. Approval of Core Director(s)
Once the project aims and budget have been approved by the MSU DD facility director(s), please have this application signed by the director(s) where this project will be completed prior to submission.

ADDRC

_____
Erika Lisabeth, Ph.D.
Director of ADDRC

IN VIVO

_____
Teresa Krieger-Burke, D.V.M., Ph.D.
Director of In Vivo Facility

MEDCHEM

_____
Edmund Ellsworth, Ph.D.
Director of MedChem Facility

Contacts:

For budget quotations or information on the overall program, please contact the director (or staff) of the core that is most relevant to your project. If you are unsure, please contact Dr. Nichols below.

MSU Drug Discovery Director
Richard Neubig, M.D., Ph.D.
rneubig@msu.edu
Phone: (517) 353-7145

MSU Drug Discovery Project Manager/Interim ADDRC Manager
Joseph Nichols, Ph.D.
DDProgram@list.msu.edu
Phone: (517) 353-2483

MSU ADDRC Director
Erika Lisabeth, Ph.D.
matheser@msu.edu
Phone: (517) 432-4507

MSU In Vivo Facility Director
Teresa Krieger-Burke, D.V.M., Ph.D.
invivo@msu.edu
Phone: (517) 432-7763

MSU Medicinal Chemistry Facility Director
Edmund Ellsworth, Ph.D.
ellswo59@msu.edu
Phone: (810) 623-5430

Target Product Profile (TPP)

- Defines the clinical and commercial criteria for discovering and developing a successful drug
- Defines the minimum and optimum criteria for the drug discovery project
- Provides a shared vision for the direction of a project
- Can and should be modified during the lifetime of the project to address changing opportunities
- ***Not all items will be known early in the project. Information available will grow with time***
- ***Screening programs may not have as much information as advanced programs.***

Template 1 (Therapeutics)

Item	Comments/Data
Market – Therapeutics (human or companion animal)	
Primary Indication (Note if there are secondary indications)	
#Patients and type (human or which animal species)	
Existing Agents for Indication and weaknesses (Key question- Do current therapies meet clinical needs?)	
Anticipated market value if known.	
Biology	
Mechanism of Action (MOA) or phenotype	
Biomarkers (Identified)	
Clinical Do-ability – Can the mechanism be tested clinically? (Yes or No, path forward)	
Risks (selectivity, development of resistance, etc.)	
Safety	
Equivalent or improved safety over existing agents? Yes or No. Explain	
Safety risks vs. benefits considerations	
Other considerations?	
Drug Profile	
If known, candidate series and structure (or series to be pursued) if known. Is it suitable as a drug or probe (physical properties, rule-of-5, etc.)	
Acceptable / Required modes Administration (IV, SubQ, IP, Oral, Topical, Other)	

Intellectual Property	
Patents filed or to be filed, Invention disclosures filed with MSU (if program has advanced to this level)	
Plan to patent filing	

Template 2 (Agricultural)

Item	Comments/Data
Market - Agricultural (Veterinary, Crop and Food Security)	
Primary application (Note if there are secondary uses)	
#Patients (cattle, swine, chickens, hectares of land, etc.)	
% not responding to existing products	
Existing compounds for application and weaknesses. How will this product address weaknesses?	
Required efficacy (% survival, increase in yield, etc.)	
Anticipated market value (MSU Technologies) – Have there been discussions with MSU Technologies?	
Biology	
Mechanism of Action (MOA) or phenotype	
Biomarkers (Identified?)	
Clinical Do-ability – Can the mechanism be tested in the field? (Yes or No, path forward)	
Other features? (development of resistance, etc.)	
Safety	
Need for equivalent or improved safety over existing agents? (User, environmental, etc.) Yes or No. Explain	
Required withdrawal periods (if feed animal)	
Safety risks vs. benefits considerations	
Agent Profile	
Candidate compound and *structure* (or series to be pursued) if known	
Acceptable / Required modes of use or application.	
Use frequency (Single or multiple application)	
Intellectual Property	
Patents filed or to be filed, Invention disclosures filed with MSU	
Plan to patent filing	

Other	
Commercial Risks (Public perception, potential regulatory changes, etc.)	

Template 3 (Technology)

Item	Comment / Data
Market – Technology	
Primary application (Note if there are secondary uses)	
Market size	
Are there competing technologies? Weaknesses? How can they be addressed with this technology?	
Required increases in efficiency, delivery, etc. (% survival, increase in yield, etc)	
Anticipated market value (MSU Technologies) – Have there been discussions with MSU Technologies?	
Technology	
Description of technology	
Do-ability – How can the technology be applied?	
Safety	
Need for equivalent or improved safety over existing tech. (User, environmental, etc.) Yes or No. Explain	
Safety risks vs. benefits considerations	
Intellectual Property	
Patents filed or to be filed, Invention disclosures filed with MSU	
Plan to patent filing	
Other	
Why would this product would be used over existing tech?	
Commercial Risks (Public perception, potential regulatory changes, etc.)	

Example of completed Target Project Profile

**delete in submitted version*

Item	Comment / Data
Market – Therapeutics (human or companion animal)	
Primary Indication (Note if there are secondary indications)	Skin and Soft tissue infections (>$1 billion). Secondary – Diabetic foot MIC90s (Clinical Pathogens) • Indication 1 -S.aureus (<0.25 ug/mL) – primary pathogen of interest
#Patients	80,000 human patients / yr.
Existing Agents for Indication and weaknesses	Zyvox -oxazolidinone ($ 2 billion in sales but going off patent). New agent will have to compete with a generic. Little development of antimicrobial resistance seen in clinic
Anticipated market value (MSU Technologies)	$300 million 5th yr sales
Biology	
Mechanism of Action (MOA) or phenotype	RNA polymerase; Frequency of resistance < 10^{-8}
Biomarkers (Identified)	Reduction of bacterial load (disease)
Clinical Do-ability – Can the mechanism be tested clinically? (Yes or No, path forward)	Yes. A number of antibacterial agents have been tested clinically. Clinical program well-understood.
Other features? (i.e.; development of resistance)	No cross-resistance to any known class of antibacterials.
Safety	
Equivalent or improved safety over existing agents? Yes or No. Explain	Peptides are generally safer than other classes of drugs. No bone marrow toxicity expected as typically seen with Zyvox.
Safety risks vs. benefits considerations	Safety- improved over Zyvox against two or more of the following. No worse for the others. • severe diarrhea • fungal infections • thrombocytopenia • myelosuppression • serotonin syndrome • neuropathies • angioedema Regulatory advantage would be antimicrobial activity against pathogens not susceptible to front-line therapy. Although providing regulatory advantage, no marketing value would be realized

	w/o an increase resistance in clinical setting (>20%).
Other considerations?	
Drug Profile	
Candidate compound and *structure* (or series to be pursued) if known	Cyclopeptides (8-amino acids)
Acceptable / Required modes Administration (IV, SubQ, IP, Oral, Topical, Other	IV with step-down to oral.
Dosing Frequency (Once-a-day, twice-a-day, etc.)	IV in hospital setting with stepdown therapy to oral (2X / day).
Intellectual Property	
Patents filed (application #) or to be filed, Invention disclosures filed with MSU	Invention disclosure filed May 2017.
Plan to patent filing	Patent to be filed June 2018 (Composition of matter)
Other	
Commercial Risk	• Reserved for second line therapy due to concerns over resistance development • Agent doesn't meet superiority requirements for efficacy. May impact potential value.