***Request for Applications*: Assemble a pre-Investigational New Drug meeting package in compliance with United States Food and Drug Administration requirements for a drug microarray patch and lead an initial FDA meeting in Q1 2021, in preparation for a future phase 1 clinical study - PATH RFA# 2020-010**

Questions and answers

Question	Answer
1. Is the proposal for a fixed-fee or time-and-materials contract?	It will be a cost reimbursement subaward.
2. Should we include (in the proposal) ongoing RA strategic assessment, CMC, and toxicology support also in the RFP?	Yes.
3. Is this technology being used currently in a similar way or is this a novel use?	Dissolving MAPs which deliver drugs are not currently licensed by the FDA, but some clinical trials of other developers' products have been conducted.
4. As cabotegravir is currently under development in other formulation/presentations, will the non-clinical/clinical information developed to support those programs, if applicable, be available for review in support of development of the safety profile for the proposed microneedle formulation?	Yes.
5. What is your team's recent experience with FDA interactions and drug/device development process at the IND stage?	PATH has experience with FDA interactions and drug/device development at the IND stage, but not related to this product.
6. Does PATH require a face-to-face meeting with FDA?	No, PATH does not require a face-to-face meeting with the FDA, but please include a face-to-face meeting in your budget.
7. If FDA only grants a teleconference or Written Responses Only, will the allotted time for face-to-face meeting be allowed to be transferred to these tasks?	Yes.
8. Does the microarray patch have a 510(k) clearance or PMA approval, or been approved with another drug(s) product?	No.
9. Does the formulation have any novel excipients?	The MAP formulation includes GRAS excipients only, such as PVA and PVP. Formulation details will be provided to the selected regulatory organization (after a confidential disclosure agreement is executed).
10. Typically, Investigator's Brochures are not provided in pre-IND submissions. Please confirm that this will be required after the pre-IND Meeting, in parallel with the draft clinical protocol.	Correct; we do not need the IB for the pre-IND meeting. However, we would like to prepare a draft IB in preparation for future steps. The draft IB can be developed in parallel with the draft clinical protocol and completed after the pre-IND meeting.
11. Please confirm that an IND submission is not part of this scope.	Correct; an IND submission is not part of the scope.
12. Regarding the pharmacology/toxicology test plan, please clarify whether the chosen vendor should anticipate providing guidance/support for the development of appropriate non-clinical study plan to support the pre-IND meeting and subsequent opening of IND for initiation of Phase 1 studies?	If your organization has the capability to support pharmacology/toxicology study design, please include and describe this capacity in your proposal; this is a desired but not required qualification.
13. Regarding attendance/presentation at the pre-IND meeting, please clarify if the chosen vendor should anticipate providing appropriate subject matter expert to represent non-clinical, clinical and CMC in addition to PATH/CMO representatives?	If your organization has the capability to support non-clinical, clinical, and CMC in the pre-IND meeting, please describe this capacity in your proposal; this is a desired but not required qualification.

Question	Answer
14. Will you be assisting in development of clinical aspects of IND prep/protocol prep?	Yes, PATH will assist in the development of clinical aspects of the pre-IND preparation and protocol preparation, but expects the selected regulatory organization to lead the effort.
15. Where do you intend to run their clinical trial (i.e., US or ex US)?	We expect the future, initial clinical trial to be conducted in the US.
16. Do you currently have a list of questions for which you are seeking FDA feedback, or are you looking for RCA to define based on total data package available?	PATH does not have a list of questions; the selected regulatory organization is expected to work with us to develop a list of questions.
17. Have you approached FDA yet for a designation of primary mode of action for the combination product, (i.e. do you know yet if FDA will assign review of product to CDER or CDRH?)?	No, we have not approached the FDA yet for designation, but we expect that CDER will have jurisdiction.
18. The following items on your list will need a clinical pharmacologist or clinical trial MD. Do you need assistance with this, or do you already have a CRO selected? (Typically, the CRO will develop the clinical trial protocols, toxicology plans and clinical synopsis)? • Pharmacology/toxicology test plan • Preclinical pharmacology data and test plan • Clinical synopsis for the pre-IND consultation • Draft clinical trial protocol, following confirmation of the clinical trial synopsis during the pre-IND consultation • Investigator's Brochure	Yes, we will need assistance with this.
19. What pre-clinical data is available currently (i.e., do you have adequate studies to support safety/toxicology/dosing in humans)?	We have preliminary (non-GLP) preclinical data to demonstrate initial pharmacokinetics in rats currently available. We do not have adequate studies to support safety/toxicology/dosing in humans yet.
20. Do you have an organization identified such as CRO that will be developing your clinical trial protocol, or clinical trial requirements, etc. (and who)?	No; the selected regulatory organization should anticipate assisting PATH to identify a suitable CRO.
21. Has your CRO/CMO organizations been thru a satisfactory FDA inspection yet?	We have not selected a contract manufacturer or contract research organization yet.
22. Is the manufacturing process well defined and have you performed any process validation as yet? How soon can you manufacture to support clinical trial products?	We are currently in the process of choosing a CMO to define the manufacturing process and help prepare the CMC data package that will be part of the pre-IND consultation. Clinical trials are a future step that are not within the scope of our current funding.
23. Are the analytical methods in place to support evaluation of clinical samples analysis?	No.

MAPs for PrEP manufacturing/regulatory scope: objectives, roles, and responsibilities

Objective 1: To establishing a current Good Manufacturing Process (cGMP) small-scale manufacturing process for microarray patches (drug-specific) and prepare a chemistry, manufacturing, and controls (CMC) data package for a pre-Investigational New Drug (pre-IND) submission.

Objective 2: To assemble a pre-IND meeting package in compliance with United States Food and Drug Administration (FDA) requirements for a drug microarray patch and lead an initial FDA meeting in Q1 2021, in preparation for a future phase 1 clinical study.

Partners and roles
PATH: MAPs for PrEP project lead and liaison with the donor.
Queen's University Belfast (QUB): academic institution leading technical development of CAB MAPs.
Contract manufacturing organization (CMO): focused on Objective 1 activities.
Contract regulatory support organization (CRSO): focused Objective 2 activities.

Definitions
Responsible: responsible for performing the task.
Accountable: accountable for the task being completed.
Consulted: consulted prior to the activity being performed.
Informed: informed that the task has been completed.

Activity	Responsible	Accountable	Consulted	Informed
Technology transfer from QUB to the CMO, including transfer of analytical methods and formulation details.	CMO	PATH	QUB	CRSO
Document process; any outstanding requirements.	CMO	PATH	QUB	CRSO
Site visits as necessary.	CMO	PATH	QUB	CRSO
Conduct gap analysis and draft plans for establishing a small-scale cGMP process.	CMO	PATH	QUB	CRSO
Document gap analysis and draft manufacturing plans to share with the team.	CMO	PATH	QUB	CRSO
Review/discuss gap analysis and draft manufacturing plans with the team.	CMO	PATH	QUB	CRSO
Revise/finalize gap analysis and draft manufacturing plans.	CMO	PATH	QUB	CRSO
Conduct process development	CMO	PATH	QUB	CRSO
Procure molds.	CMO	PATH	QUB	CRSO
Develop GMP process.	CMO	PATH	QUB	CRSO
Review/discuss process development documentation with the team.	CMO	PATH	QUB	CRSO
Implement manufacturing process.	CMO	PATH	QUB	CRSO
Produce test batches of GMP-like placebo MAPs.	CMO	PATH	QUB	CRSO
Document batch results.	CMO	PATH	QUB	CRSO
Review/discuss draft results with the team.	CMO	PATH	QUB	CRSO

Activity	Responsible	Accountable	Consulted	Informed
Revise process as necessary.	CMO	PATH	QUB	CRSO
Validate process.	CMO	PATH	QUB	CRSO
Produce test batches of GMP-like CAB MAPs.	CMO	PATH	QUB	CRSO
Document batch results.	CMO	PATH	QUB	CRSO
Review/discuss draft results with the team.	CMO	PATH	QUB	CRSO
Revise process as necessary.	CMO	PATH	QUB	CRSO
Validate process.	CMO	PATH	QUB	CRSO
Pre-IND consultation meeting with the FDA.	CRSO	PATH	CMO	QUB
LOGISTICS	CRSO	PATH	CMO	QUB
Develop a strategy and key questions.	CRSO	PATH	CMO	QUB
Review/discuss strategy and key questions with team.	CRSO	PATH	CMO	QUB
Revise/incorporate edits to the strategy and key questions.	CRSO	PATH	CMO	QUB
Outline the process for the pre-IND meeting, list of required materials, participants, and establish a timeline.	CRSO	PATH	CMO	QUB
Review/discuss the process for the pre-IND meeting, list of required materials and participants, and timeline with team.	CRSO	PATH	CMO	QUB
Revise and implement process (set up bi-weekly meetings to coordinate development of documents).	CRSO	PATH	CMO	QUB
CONTENT	CRSO	PATH	CMO	QUB
1. Draft an outline of the clinical/regulatory plan.	CRSO	PATH	-	QUB, CMO
Review/discuss with team.	CRSO	PATH	-	QUB, CMO
Revise/incorporate edits to the clinical/regulatory plan.	CRSO	PATH	-	QUB, CMO
Finalize clinical/regulatory plan for pre-IND consultation.	CRSO	PATH	-	QUB, CMO
2. Draft an outline of the CMC package.	CMO	PATH	QUB, CRSO	-
Review/discuss with team.	CMO	PATH	QUB, CRSO	-
Revise/incorporate edits to the CMC package.	CMO	PATH	QUB, CRSO	-
Finalize CMC package for pre-IND consultation.	CMO	PATH	QUB, CRSO	-
3. Draft an outline of the pharmacology/toxicology test plan.	CRSO (desired)	PATH	CMO, QUB	-
Review/discuss with team.	CRSO (desired)	PATH	CMO, QUB	-
Revise/incorporate edits to the pharmacology/toxicology test plan.	CRSO (desired)	PATH	CMO, QUB	-
Finalize pharmacology/toxicology test plan for pre-IND consultation.	CRSO (desired)	PATH	CMO, QUB	-
5. Draft the clinical study synopsis.	CRSO	PATH	-	QUB, CMO

Activity	Responsible	Accountable	Consulted	Informed
Review/discuss with team.	CRSO	PATH	-	QUB, CMO
Revise/incorporate edits to the clinical study synopsis.	CRSO	PATH	-	QUB, CMO
Finalize clinical study synopsis for pre-IND consultation.	CRSO	PATH	-	QUB, CMO
HOLD PRE-IND MEETING	CRSO	PATH	CMO	QUB
Request and schedule a pre-IND consultation with the FDA.	CRSO	PATH	CMO	QUB
Prepare the team to meet with the FDA.	CRSO	PATH	CMO	QUB
Lead the meeting with the FDA.	CRSO	PATH	CMO	QUB
Provide pharmacology/tox expertise in FDA meeting	CRSO (desired), PATH, QUB	PATH	-	CMO
Provide CMC expertise in FDA meeting	CMO, CRSO (desired)	PATH	-	QUB
Provide regulatory expertise in FDA meeting	CRSO; PATH	PATH	CMO	QUB
Provide clinical expertise in FDA meeting	CRSO	PATH	CMO	QUB
Write meeting minutes and debrief with the team afterwards.	CRSO	PATH	CMO	QUB
Review/discuss meeting minutes team.	CRSO	PATH	CMO	QUB
Revise/incorporate edits to the meeting minutes.	CRSO	PATH	CMO	QUB
Finalize meeting minutes.	CRSO	PATH	CMO	QUB
Conduct any required follow-up with the FDA.	CRSO	PATH	CMO	QUB
Draft clinical trial protocol.	CRSO	PATH	CMO	QUB
Draft clinical trial protocol.	CRSO	PATH	CMO	QUB
Revise/incorporate edits to the clinical trial protocol.	CRSO	PATH	CMO	QUB
Finalize draft clinical trial protocol.	CRSO	PATH	CMO	QUB
Draft Investigator's Brochure (as a preparatory step for a future IND).	CRSO	PATH	CMO, QUB	-
Draft Investigator's Brochure	CRSO	PATH	CMO, QUB	-
Revise/incorporate edits to the Investigator's Brochure.	CRSO	PATH	CMO, QUB	-
Finalize draft Investigator's Brochure.	CRSO	PATH	CMO, QUB	-
Project close.	CRSO & CMO	PATH	QUB	-
Finalize documents.	CRSO & CMO	PATH	QUB	-
Share all documents with team.	CRSO & CMO	PATH	QUB	-
Complete required activities to close out the project.	PATH	PATH	QUB, CRSO, CMO	-

Abbreviations: CAB, cabotegravir; CMC, chemistry, manufacturing, and controls; CMO, contract manufacturing organization; CRSO, contract regulatory support organization; FDA, United States Food and Drug Administration; GMP, Good Manufacturing Practices; IND, Investigational New Drug; MAPs, microarray patches; QUB, Queen's University Belfast.