REQUEST FOR PROPOSAL (RfP)

Title: Request for proposal for grants to support development, regulatory filing, and commercialization of pediatric Darunavir/Ritonavir 120/20 mg fixed dose combination tablets

0013-Peds DRV/r

Issue Date: September 14, 2020

Deadline for Questions: September 24, 2020, 5pm EDT

Closing Date: October 16, 2020, 5pm EDT
1. **Summary**

This request for proposal (RfP) is to solicit competitive bids for grants to accelerate the development and commercialization of a generic pediatric darunavir/ritonavir 120/20 mg fixed dose combination solid oral dose tablet (DRV/r 120/20 mg FDC tablet), where the ritonavir is heat-stabilized using suitable technology (e.g., hot melt extrusion (HME)).

To be considered for this grant, the supplier must have a demonstrably viable plan to develop the pediatric DRV/r FDC product as well as prior experience in commercialization of products.

The goal of this program is for a generic pharmaceutical manufacturer (“Manufacturer”) to develop a commercially viable pediatric DRV/r 120/20 mg product and obtain tentative US FDA approval or WHO Prequalification. This pediatric DRV/r 120/20 mg product is intended to be used as a World Health Organization (WHO) recommended alternative second- and third-line treatment for children (> 10 kg/3 years and older) living with HIV in low- and middle-income countries (LMICs). CHAI estimates have shown that once this product is available in LMICs, between 25,000 to 70,000 children could benefit annually from this product.

2. **About CHAI and Unitaid**

The Clinton Health Access Initiative, Inc. (CHAI) is a global health organization committed to catalyzing access to high-quality, low-cost drugs and diagnostics and strengthening integrated health systems in resource-limited settings.

CHAI is committed to increasing the affordability of and accelerating access to optimal ARV therapies in designated LMICs through a Unitaid-funded project entitled ‘Accelerating Patient Access to Optimal Antiretrovirals (Optimal Project)’. This project is geared towards developing interventions that will:

- Accelerate time to market for innovative new products; and
- Generate early demand and rapid uptake from working with country HIV programs in a set of focal countries.

Unitaid is an international organization that invests in new ways to prevent, diagnose, and treat HIV/AIDS, tuberculosis, and malaria more quickly, cheaply, and effectively. For more information on Unitaid, please visit: [www.unitaid.org](http://www.unitaid.org).

*Please note that all RfP enquiries should be in writing and directed to the designated email address in this RfP.*

*CHAI and Unitaid will not respond to related enquiries via telephone or other communication platforms.*
3. Summary of Target Product

The target product for this RfP is a generic pediatric darunavir/ritonavir 120/20 mg fixed dose combination solid oral dose tablet (DRV/r 120/20 mg FDC tablet) containing 120 mg darunavir and 20 mg ritonavir.

Darunavir (DRV) is a best-in-class protease inhibitor, and when boosted with ritonavir (RTV, r), DRV is proven to be an effective treatment for HIV patients with multiple drug resistance. Superior clinical efficacy, favorable tolerability and toxicity profile, and a high genetic barrier to resistance makes DRV/r an optimal second-line antiretroviral (ARV) drug for adults, adolescents, and pediatrics aged 3 years and older.\(^1\) The WHO’s updated treatment guidelines\(^2\) include DRV/r in combination with an optimized NRTI backbone as the alternative second-line regimen for adults, adolescents, and children (3 years and older) living with HIV for whom DTG-based regimens have failed. DRV was first approved for adult use by the US FDA in 2006. Over a decade later, neither the adult DRV/r fixed dose combination nor the pediatric DRV/r products are available. This represents a significant equity gap for people in LMICs, and there is an urgent need for product development and regulatory approval of the pediatric DRV/r product.

DRV/r 120/20 mg is identified as the most important boosted protease inhibitor formulation on the Paediatric Antiretroviral Drug Optimisation (PADO) list.\(^3\) Pediatric DRV/r 120/20 mg heat-stable tablets are included on the Expression of Interest list for WHO Prequalification.

4. Statement of Work

This scope of work includes the following activities:

- Manufacturer provides a report to CHAI that characterizes the DRV and RTV APIs to be used for this project;
- Manufacturer develops the DRV/r 120/20 mg FDC formulation, including formulation development, manufacturing process scale-up, analytical method development and validation, physical product characterization, bioequivalence studies, and stability studies;
- Manufacturer prepares and submits a regulatory dossier for the US FDA PEPFAR Tentative Approval Program and WHO Prequalification;
- Manufacturer prepares and submits a plan for regulatory filings in CHAI’s priority list (see priority country list in Annex 3) and adheres to the elements of this plan, including clear timelines; and
- Manufacturer prepares a production and supply plan that ensures capacity to supply qualified orders (minimum size to be determined as part of the project plan) with manufacturing lead time of no more than 90 days.

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1. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3218677/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3218677/)
The development support grant offered by CHAI through the Unitaid Optimal program is designed to offset a portion of the manufacturer’s development and commercialization costs.

Under the proposed agreement, the Manufacturer must agree to an access price and associated terms and supply conditions that is acceptable to public sector procurement groups in the target LMICs, including the countries themselves, which will be included in the contracts between the manufacturer and CHAI. This access price should be immediately effective from the day an agreement is concluded and signed by all parties.

5. Instructions to interested parties
   a. RfP
      i. All proposals should be submitted in English and signed by an authorized representative of the Responder (Form A in Annex 1).
      ii. Proposals should be submitted via email with the subject line RfP–Peds DRV/r to: pediatricrfp@clintonhealthaccess.org.
      iii. Proposals received after the stipulated closing date will be deemed invalid.
   b. Timeline
      The timeline for the RfP process is described below. Proposals received after the deadline will not be considered.

      | Event                                      | Date                  |
      |--------------------------------------------|-----------------------|
      | RfP Released                               | September 14, 2020    |
      | Information Session                        | September 17, 2020, 4pm IST/12:30pm CEST/6:30am EDT |
      | Q&A Period for Manufacturers                | September 14-24, 2020 |
      | Q&A Response Document Released             | September 29, 2020    |
      | Proposals Due                              | October 16, 2020, 5pm EDT |

   c. Question and answer
      i. A formal period during which questions regarding this RfP are answered will be held for eleven days following the posting of the RfP on CHAI’s website. Questions should be addressed to: pediatricrfp@clintonhealthaccess.org.
      ii. A formal information session to answer questions related to the RfP process will be held on Thursday, September 17, 2020, at 4pm IST/12:30pm CEST/6:30am EDT. Please use the Zoom meeting invitation below:

      CHAI is inviting you to a scheduled Zoom meeting. You are encouraged to join via the web link below to both experience optimal connectivity as well as to not incur additional charges.
      Join from PC, Mac, Linux, iOS or Android:
      https://chai.zoom.us/j/6089920784?pwd=TIMwUjJlRWGIUEhIKZThjSVU3ZmJpdz09
      Password: 025870
Or iPhone one-tap (US Toll): +13126266799,6089920784# or +16468769923,6089920784#
Or Telephone:
Dial:
+1 312 626 6799 (US Toll)
+1 646 876 9923 (US Toll)
Meeting ID: 608 992 0784
Password: 025870
International numbers available: https://chai.zoom.us/u/acWwZpo2Kp

iii. Enquiries must be received by the stipulated deadline. All questions and answers will be published on the CHAI website.
iv. Telephone enquiries are not be permitted.

d. Eligibility
The RfP is open to companies who meet the following criteria:
• Manufacturers have previously submitted dossiers to a regulatory authority and received tentative or full approval for products;
• Manufacturers’ production facilities operate under current Good Manufacturing Practice (cGMP) as established by the International Conference on Harmonization (ICH);
• Manufacturers must agree to share any recent regulatory authority inspection reports (e.g., from an SRA or WHO PQ) and subsequent correspondence related to major or critical observations, including corrective and preventative action plans, if they are selected for the award;
• Manufacturers must agree to host and pass an independent quality audit if they are selected as a finalist for the award; and
• Manufacturers will agree to establish a project team structure that includes CHAI participation as well as host regular meetings (in person or via telecom) as/when required.

e. Costs of preparing documents
All costs associated with preparing and submitting a proposal will be borne by the Responder.

f. Confidentiality
Information which the Responder considers to be proprietary should be clearly marked as such. All such information will be treated as confidential and used by the CHAI team for assessment purposes only.

g. Disclosure
Information relating to the examination, clarification, and evaluation of responses shall not be disclosed to Responders or any other persons not officially concerned with such process.
h. Terms and Conditions
Although terms and conditions for the development contract will be finalized during the negotiation process after final manufacturer(s) have been selected, a sample of CHAI’s standard terms and conditions has been attached to this document (Annex 2) for reference. A formal agreement including these terms will be executed by CHAI and the selected Manufacturer prior to initiation of the grant.

6. Proposal requirements
Responders should provide the following information in the proposal response to this RfP:
   a. Completed forms found in Annex 1: A (Response to RfP) and B (Quality Audit Agreement);
   b. Completed RfP Excel questionnaire – separate attachment to RfP; and
   c. Separate Word document outlining the supplier’s development plan and timeline for the activities described in the statement of work, Section 4 above. Included in this document should be a discussion of the supplier’s capacity to manufacture the DRV/r 120/20 mg FDC tablet, a timeline (or Gantt chart) highlighting the milestones indicated in the Timeline tab of the RfP questionnaire, and the strategy for ensuring sustained supply in LMICs. This document should be no longer than five pages in length.

CHAI reserves the right to request additional information, arrange interviews with the Responder, visit the Responder’s premises and facilities, and conduct an audit to verify the information provided.

7. Evaluation Criteria
To be considered for an award, the manufacturer must demonstrate the necessary experience of commercializing pediatric HIV drugs, necessary experience of commercializing products manufactured with the intended technology, a license from MPP or AbbVie to manufacture RTV at the time of award, and experience registering and supplying generic ARV drugs to the focal countries.

CHAI will assess each eligible proposal based on selection criteria that includes the overall quality of the development and commercialization plan provided, timelines, corporate capabilities and demonstrated expertise with similar products, and proposed estimated budget. CHAI anticipates that several companies will be identified for further discussions to refine project plans, timelines, and cost estimates.

CHAI will engage with a third party to perform a quality audit of the selected supplier. CHAI anticipates making a grant award to one supplier in Q1 2021. Based on the current anticipated timeline, it is expected that the awarded manufacturer will file for generic regulatory approval by 2024, although this is subject to change.
Annex 1: Forms to be Completed by Responders

FORM A: Response to RfP

This form must be completed, signed, and returned to CHAI at pediatricrfp@clintonhealthaccess.org.

DECLARATION
We, the undersigned, having read the RfP for pediatric darunavir/ritonavir (DRV/r) 120/20 mg FDC tablets, submit our proposal, which includes the information requested in Section 5. We confirm that all the information provided is correct.

We confirm that we are interested in entering into discussions for a possible collaboration with CHAI on the development, manufacture, filing to FDA, and commercialization of pediatric darunavir/ritonavir (DRV/r) 120/20 mg FDC tablets according to the terms of this RfP.

We understand that CHAI’s issue of the RfP and the proposal we submit is not a commitment by either party to enter into such discussions or collaboration. We further understand that CHAI reserves the right to discuss and collaborate with one or multiple parties, no parties, or to cancel the RfP at its sole discretion.

This RfP and any proposals thereto shall be the property of CHAI.

Name of authorized representative:

Title:

Signature:

Date:

Company name:

Postal Address:

Telephone No.:

Email Address:
FORM B: Quality Audit Agreement

This form must be completed, signed, and returned to CHAI at pediatricrfp@clintonhealthaccess.org.

DECLARATION
Responder agrees that if selected for the RfP award, permission will be given to CHAI to conduct a quality audit in order to assess that the supplier is operating under cGMP.¹ This will be a general GMP and Quality Systems audit, most likely performed by an independent third-party consultant. This audit will be scheduled directly with the supplier after the award has been granted.

Name of authorized representative: 

Title: 

Signature: 

Date: 

Company name: 

¹ Valid cGMP authorities include SRAs and regulatory authorities participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S). For PIC/S, please refer to www.picscheme.org. An SRA is defined as a regulatory authority that is (1) a Founding (USA, European Commission, Japan) or Standing (Canada, Switzerland) Regulatory Member of the International Conference on Harmonisation (ICH); or (2) a Standing Observer (WHO, The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)) as specified on www.ich.org. In addition, countries that have mutual recognition with one of the Founding Regulatory Members (e.g., EMA has mutual recognition with Australia and New Zealand) are considered SRA.
Annex 2: CHAI’s Standard Terms and Conditions for Contracts

Sample Standard Terms and Conditions for CHAI Contracts

The Manufacturer will come to an agreement with CHAI on the terms of the commercialization support and the milestones that need to be reached for funding to be provided by CHAI. This will include regular financial and product-specific milestone reporting requirements. CHAI will determine disbursement requirements.

In addition to the terms and conditions in Activity 2.3 of the Project Plan relating to the product for which they are receiving commercialization support (“Product”), representations and warranties on the quality, safety, and compliance of the Product, confidentiality, and other standard terms and conditions, the Commercialization Support Agreement between CHAI and Supplier will include these sample terms:

1. Manufacturer agrees that it shall meet the following qualifications at all times during the Term of the Agreement and for the duration of its participation in the Project:
   a) **Manufacturing Quality** Compliance with WHO (Geneva) or FDA GMP standards applicable to the manufacture or supply of the Product, including, but not limited to, adherence to certain minimum manufacturing and quality control standards necessary for Supplier to manufacture and supply the Product as well as possession of all applicable certifications and approvals from any certifying industry organization or national regulatory authority.
   b) **Financial Stability** Maintenance, on a financial basis, of positive net worth and adequate cash flow to ensure that Supplier is capable of paying for the resources necessary for Supplier to manufacture and supply the Products.
   c) **Compliance with Laws** Compliance with all applicable laws, regulations, and conditions relevant to Supplier’s operations and performance under the Commercialization Support Agreement.
   d) **Compliance with Labor Codes** Compliance with its Internal Code of Conduct that is compliant with the International Labor Organization’s “Standards and Fundamental Principles and Rights at Work” and the Fair Labor Association’s “Workplace Code of Conduct”.

2. Indemnification. Supplier agrees to indemnify, defend, and hold UNITAID, WHO, and CHAI (“Indemnified Parties”) harmless from and against any claims, losses, liability, obligations, lawsuits, deficiencies, damages, or expenses of whatever nature, whether known or unknown, accrued, absolute, contingent or otherwise, including, without limitation, interest, penalties, attorney's fees, costs of investigation and all amounts paid in defense or settlement of the foregoing (collectively, “Loss”), suffered or incurred by the Indemnified Parties as a result of the occurrence of, or arising out of, any breach of this Agreement by Supplier, including, but not limited to, any of Supplier’s representations and warranties contained herein.
   a) Manufacturer also agrees to indemnify, defend, and hold the Indemnified Parties harmless from and against any Loss suffered or incurred by the Indemnified Parties arising out of or relating to any (i) third-party product liability claim against any Product; (ii) defects in any Product supplied; or (iii) non-compliance by such manufacturer or supplier with any technical requirements applicable to any Products supplied.
b) Manufacturer also agrees to indemnify, defend, and hold the Indemnified Parties from and against all claims, damages, losses, costs, and expenses arising out of the alleged infringement of a patent, design, tradename, or trade-mark arising under or relating to the Commercialization Agreement.

3. Dispute Resolution. Any dispute arising out of or relating to the Commercialization Support Agreement or the transactions contemplated hereby or any breach of the same shall be settled by final and binding arbitration. Any arbitration conducted pursuant to this provision shall be conducted in New York, New York, USA, and shall be conducted in the English language in accordance with the International Arbitration Rules established by the American Arbitration Association.

4. Loss, Fraud, Bribery, Corruption and Conflicts of Interest
   a) The Parties confirm that no official, employee, or officer of the other Party has received or will be offered any individual benefit arising from this Agreement.
   b) The Manufacturer will take all measures to prevent conflicts of interest arising that may have an impact on the implementation of the Project and will promptly declare to CHAI and proactively manage any such conflicts of interest.
   c) The following may be deemed by CHAI to be a material breach of this Agreement: (i) failure by the Grantee to report to CHAI any known or suspected cases of loss, bribery, fraud, or other corrupt practices; (ii) confirmed serious or repeated instances of loss, bribery, fraud, or other corrupt practices; (iii) failure to declare and/or proactively manage any conflicts of interest; (iv) the giving to or receiving by an official, employee, or officer of the Manufacturer of any individual benefit in connection with this Agreement.

5. Marks
   a) This Agreement shall not be construed to grant Partner any license to use CHAI’s name or logo, both current and future, in any format (“CHAI Marks”). Any requests for use of CHAI Marks shall be submitted in writing to CHAI. CHAI shall have the right, in its sole discretion, to grant Partner any usage rights of CHAI Marks. An authorized CHAI representative must document such a grant in writing for it to be valid.
   b) CHAI exists as a separate entity from the Bill, Hillary & Chelsea Clinton Foundation (“Foundation”) to carry on and expand the projects previously conducted through the Clinton HIV/AIDS Initiative. This Agreement shall not be construed to grant Partner any license to use the name, logo, or other marks owned by the Foundation (“Foundation Marks”), in any format, including any quote, image, or likeness in any form of President Clinton, Secretary Clinton, or Chelsea Clinton (the “Clintons”). All requests for use of Foundation Marks shall be submitted in writing to CHAI. CHAI shall refer any such requests to the Clinton Foundation, which has sole discretion in granting any usage rights in Foundation Marks to Partner.

6. This Agreement shall be governed by and construed in accordance with the laws of the state of New York, without giving effect to applicable conflict of laws provisions.
Annex 3: Priority Countries (21 ‘AIDS Free’ Global Plan Priority Countries)

Angola  
Botswana  
Burundi  
Cameroon  
Chad  
Cote d’Ivoire  
Democratic Republic of Congo  
Eswatini  
Ethiopia  
Ghana  
Kenya  
Lesotho  
Malawi  
Mozambique  
Namibia  
Nigeria  
South Africa  
Tanzania  
Uganda  
Zambia  
Zimbabwe