RESEARCH COLLABORATION AGREEMENT

This Research Collaboration Agreement (this "**Collaboration Agreement**") is made and effective as of the last date of execution herein (the "**Effective Date**") by and among **Universidad Nacional de La Plata**, having offices at Facultad de Ciencias Exactas, UNLP, Calles 47 y 115 s/n, La Plata (B1900ADD), Buenos Aires, Argentina ("**UNLP**"), **Universidad Nacional de San Martin**, having offices at 25 de Mayo y Francia, C.P.: 1650. San Martín, Provincia de Buenos Aires, Argentina ("**UNSAM**") (UNLP and UNSAM, collectively, the "**Researchers**"), **Eisai Co., Ltd.**, having offices at 4-6-10 Koishikawa, Bunkyo-ku, Tokyo 112-8088, Japan ("**Eisai**"), and the **Fundación Ciencias Exactas**, with a legal address at Calle. 115 s/n of the City of La Plata (hereinafter, the "**UNLP Funds' Administrator"**). Eisai and the Researchers are sometimes referred to herein individually as a "**Party**" or, collectively as "**Parties**".

RECITALS

WHEREAS, the Global Health Innovative Technology Fund, a general association established in Japan to advance the research and development of new medicines, vaccines, and diagnostics to fight infectious diseases in the developing world, located at Ark Hills Sengokuyama Mori Tower 25F, 1-9-10 Roppongi, Minato-ku, Tokyo 106-0032, Japan ("**GHIT**") and MMV Medicines For Malaria Venture, a Swiss foundation with registration number CHE-109.363.610, located at route de Pré-Bois 20, ICC, 1216 Cointrin Geneva, Switzerland ("**MMV**"), and Eisai have entered into a Global Health Innovative Technology Fund Investment Agreement (the "**Investment Agreement**") for the research project entitled "AI-based screening for the identification of novel compounds against Chikungunya virus" (the "**Research Project**") as further described in the Exhibit A attached hereto; and

WHEREAS, in furtherance of the Research Project, Eisai is entering into this Collaboration Agreement with Researchers for the screening activities set forth in the Research Plan as further described in the **Exhibit A** attached hereto; and

NOW, THEREFORE, in consideration of the mutual promises contained herein, and having set their hands and seals hereto, the Parties hereby agree as follows:

1. **Definitions**.

1.1 "**Affiliates**" means any entity that, directly or indirectly, is controlled by, controls or is under common control with a party. For purposes of this definition, "control" means, the direct or indirect ownership of more than fifty percent (50%) of the voting or income interest in the entity, the possession otherwise, directly or indirectly, of the power to direct the management or policies of the entity, or the power to appoint fifty percent (50%) or more of the members of the governing body of the entity.

For purposes of this Agreement, an Eisai Affiliate means any entity that, now or in the future, directly or indirectly, controls, is controlled by, or is under common control with Eisai Corporation of America (or any successor entity or permitted assignee of Eisai Corporation of North America, Eisai's parent company) and/or Eisai Co., Ltd. (or any successor entity or permitted assignee of Eisai Co., Ltd., Eisai Corporation of North America's parent company) which shall include, but not be limited to: Eisai Europe Limited; Eisai Clinical Research Singapore Ptd., Ltd.; Eisai Inc.; Eisai China Inc.; and Eisai Limited.

1.2 "**Authorized Personnel**" means an employee, staff member or student of a Party who: (a) is obligated under a written agreement to (i) assign to such Party all inventions made or conceived by such individual and (ii) maintain the confidential nature of Confidential Information under terms no less stringent than the terms of this Agreement; and (b) has been apprised of the confidential nature of the Confidential Information and the Research Plan.

1.3 "**Background Intellectual Property**" means all Intellectual Property owned or controlled by any Party prior to the date of this Agreement.

1.4 "**Confidential Information**" means, collectively, the Eisai Confidential Information, UNLP Confidential Information, and UNSAM Confidential Information.

1.5 "**Data Privacy Laws**" means all applicable laws, rules and regulations governing privacy, security, data protection and the Processing of Personal Information (as defined herein), including but not limited to, the California Privacy Rights Act of 2020 ("**CCPA**").

1.6 "**Eisai Confidential Information**" means all information acquired from Eisai or generated by UNSAM and UNLP in connection with this Agreement, including, without limitation, all discoveries, inventions, patents, trade secrets, copyrights, trademarks, trade dress, and other proprietary rights relating to the Material and the Research Plan (including Intellectual Property Improvements, as herein defined), documents, records, results, reports, data, know-how, materials, compounds, assays, analytical methodologies devices or other business and/or financial and/or scientific information, objectives and strategies now known or hereafter developed (whether supplied by Eisai or otherwise) and all information generated by or provided to UNSAM and UNLP pursuant hereto, including the Materials and any copies, extracts, notes or summaries of the foregoing and any data, reports or information generated therefrom or by use thereof or other information regarding the Research Plan or other research programs being conducted by Eisai, and that such information is confidential to Eisai.

1.7 "**Intellectual Property Improvements**" as used herein and as contextually appropriate collectively or partially refers to Eisai Intellectual Property Improvements, UNSAM Intellectual Property Improvements, and UNLP Intellectual Property Improvements, each of which terms is further defined below.

1.8 "**Intellectual Property**" means all materials, ideas, products, concepts, methodologies, procedures, processes, techniques, technologies, improvements, templates, reports, information, inventions, concepts, data, know-how, compounds and other works, including Patent Rights and copyrights therein.

1.9 "**Material**" means all compounds from the Eisai compound library that are provided by Eisai to Researchers.

1.10 "**Patent Rights**" means rights in patents and/or patent applications or letters patent or the equivalent thereof issuing thereon, in any jurisdiction worldwide, and any reissues, extensions, substitutions, patents of addition, petite patents, nationalizations, continuations, divisions, and continuations-in-part applications.

1.11 "**Research Results**" means all data, documents, records, and results generated by the Parties in the performance or as a result of the Research Plan.

1.12 "**Term**" means the period commencing on the Effective Date and continuing until the completion of the Research Plan, subject to earlier termination as provided hereunder. Such term may be extended if mutually agreed in writing prior to the expiration of this Agreement.

1.13 "**UNLP Confidential Information**" means the proprietary information developed or controlled by UNLP related to the machine learning model, as well as related know-how, information, or trade secrets.

1.14 "**UNSAM Confidential Information**" means the proprietary information developed or controlled by UNSAM related to the screening assays, as well as related know-how, information, or trade secrets.

2. **Services**.

2.1 The Parties agree to share their respective Confidential Information with the other researchers and the researchers may use the Confidential Information to conduct the Research Plan.

2.2 The Parties shall carry out the activities as set forth in the Research Plan in accordance with (i) the Research Plan, (ii) this Collaboration Agreement, (iii) cGLP, and (iv) all applicable laws and regulations, including any applicable Data Privacy Laws.

2.3 During the Term UNSAM, UNLP, and Eisai's authorized representatives, shall meet confer via Electronic Meeting ("**Electronic Meeting**" shall mean meetings that can be duly convened and held in one or more separate meeting places linked together by telephone, by instantaneous audiovisual communication device or by some other instantaneous means of conferring for the dispatch of business) or emails from time to time, but no less than quarterly to discuss the planning and progress of the Research Plan. Before any Electronic Meeting, UNSAM and UNLP shall provide copies of all PowerPoint slides and/or notes to be used by the UNSAM and UNLP in all Electronic Meetings.

2.4 The Parties shall carry out the activities as set forth in the Research Plan in accordance with this Agreement and all applicable laws and regulations. The Researchers shall develop analyses, reports, documents, and summaries thereof as may be produced in the performance of the Research Plan, copies of which shall be provided to Eisai on a monthly basis. All raw data shall be maintained in a mutually agreed shared area, which may be provided by Eisai, and which shall be readily accessible by Eisai. A written study report, which includes all raw data obtained, a complete summary of the research carried out including an analysis and discussion of study data, results, results and conclusions, a good faith evaluation by UNSAM and UNLP of the relationship of the research to the purpose of the Research Plan, and other deliverables as may be reasonably requested by Eisai shall be submitted by UNSAM and UNLP to Eisai every six (6) months, or upon Eisai's reasonable written request.

2.5 The Parties agree that all data and reports generated under the Research Plan are subject to GHIT's Data Access Policy and the Product Access Policy available at: ghitfund.org/applyforfunding/accesspolicy/en, which GHIT may amend from time to time. Additionally, subject to Section 8.3, all packages, communications and publications related to this Collaboration Agreement, including, but not limited to, product brochures, pamphlets, posters, presentations, websites, publications, and annual reports shall indicate that the Research Plan was developed in partnership with Eisai.

3. **Materials**.

3.1 **Transfer and Ownership**. Solely to enable the conduct of the Research Plan during the term of this Agreement, Eisai will provide the Researchers with the Material. The Material shall be owned by Eisai. The Researchers agree and acknowledges that neither it nor its employees or agents shall acquire any rights of any kind whatsoever with respect to the Material as a result of performance under this Collaboration Agreement or otherwise.

3.2 **Use**. The Researchers agree to use the Material solely to conduct the Research Plan and shall not use the Material for any purpose not expressly set forth herein. The Researchers further agree not to use commercially, manufacture, or sell the Material. Additionally, the Researchers will not analyze, modify, or reverse engineer, chemically or otherwise, the Material. Unless otherwise agreed in writing by Eisai, the Researchers agree that the Material:

(a) will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects;

(b) will be used solely by Authorized Personnel only at the Recipient's facilities located at the address set forth above;

(c) will be maintained in a secure environment in a manner consistent with a standard level of care for similar materials, and with any safety or other instructions provided by Eisai;

(d) will not be transferred to anyone other than Authorized Personnel; and

(e) will be used in compliance with any written instructions provided by Eisai.

3.3 The Researchers shall take all reasonable precautions to prevent the destruction, theft, or loss of the Materials. The Researchers agree to return to Eisai all unused Materials promptly after termination or expiration of this Agreement or at any time upon Eisai's written request.

4. **Support for the Research Plan**.

4.1 Eisai shall reimburse Researchers for the performance of the Research Plan in accordance with the budget attached hereto as **Exhibit B** and made a part hereof (the "**Budget**"). The parties agree that no research shall commence, nor any liability incurred, until Eisai has confirmed in writing to UNSAM and UNLP that Eisai has received proper funding for the Research Plan under the Investment Agreement. The Researchers will act as independent contractors, and neither Eisai, nor its designee shall be responsible for any employee benefits, pensions, workers'

compensation, withholding, or employment-related taxes as to the Researchers or their personnel. No Party is obligated to spend any funds above the amount stipulated in the Budget without mutual written consent of all the Parties.

4.2 UNSAM and UNLP shall submit invoices to Eisai, which invoices shall either detail the agreed upon costs being invoiced, including startup costs, or reflect a breakdown of the services performed, the total amount due for each such service, and the total amount due for all services. All invoices shall state the amount due in Japanese Yen (¥). Eisai shall pay the invoicing party any undisputed amounts specified in such invoices within forty-five (45) days of its receipt of such invoices. Any purchase order issued by Eisai in connection with this Collaboration Agreement will be for payment purposes only, will not be deemed a contract document, and its terms and conditions shall not apply to any Party.

4.3 Eisai shall not be responsible for any unauthorized charges or expenses incurred by the Researchers. The Researchers shall maintain books and records supporting all fees and reimbursable expenses and shall permit Eisai or its independent public accountants to inspect such books and records to verify amounts invoiced hereunder, provided any such inspection may only take place during the Term, during regular business hours, and with reasonable advanced notice.

4.4 All payments made under this Collaboration Agreement will be in Japanese Yen (¥). Notwithstanding anything to the contrary herein, Eisai, in its sole discretion, may authorize changes to the payment and reporting schedules from time to time . Eisai will confirm any such changes in writing. Eisai or its designee will assess progress against the Research Plan and based on this assessment may determine that amendments may be required as a prerequisite to receiving additional payments. The Research Plan staff of each of the Parties will be provided reasonable advance notice of such in-person meetings, and the Researchers will cooperate with all reasonable requests for assistance or documentation.

4.5 The Parties acknowledge and agree that all payments hereunder are contingent on UNSAM and UNLP providing invoices which describe all activities performed for which payment is sought, including a description of the scope and nature of services performed, billing period (time period of charges) and UNSAM and UNLP's tax identification number, and shall be accompanied by appropriate supporting documentation as reasonably requested by Eisai.

4.6 Any unused or uncommitted funds from the Budget must be returned to Eisai within fifteen (15) days following the completion of the Research Plan, or earlier upon Eisai's written request.

4.7 All funds allocated to UNSAM (Universidad Nacional de San Martín) under this Agreement shall be managed and administered exclusively by the Fundación Instituto de Investigaciones Biotecnológicas (the "Foundation"). The Foundation shall oversee the receipt, allocation, and disbursement of such funds in accordance with applicable laws and regulations, as well as the terms and conditions of this Agreement. The Foundation shall maintain accurate financial records and provide periodic reports as required by the Parties

4.8 All funds allocated to UNLP (Universidad Nacional de La Plata) under this Agreement shall be managed and administered exclusively by the Fundación Ciencias Exactas, Funds' Administrator. The UNLP Funds' Administrator shall oversee the receipt, allocation, and disbursement of such funds in accordance with applicable laws and regulations, as well as the terms and conditions of this Agreement. The UNLP Funds' Administrator shall maintain accurate financial records and provide periodic

reports as required by the Parties.

5. **Term and Termination**.

5.1 This Collaboration Agreement shall be deemed effective as of the Effective Date and shall continue in effect until the earlier of: (i) five (5) years from the Effective Date; or (ii) the date the Research Plan has been completed (the "**Term**").

5.2 Eisai may terminate this Collaboration Agreement with immediate effect in the event the Investment Agreement expires or is terminated.

5.3 Eisai may at any time and without cause terminate this Collaboration Agreement by giving thirty (30) days written notice of termination to Researchers. The Parties agree to fully cooperate with the Eisai in the event of termination.

5.4 Each Party may terminate this Collaboration Agreement in the event of the material breach of the terms of this Collaboration Agreement by any Party, which breach is not cured within thirty (30) days after the receipt of written notice from the non-breaching Party to the breaching Party and any other non-breaching Party, specifying the nature of the breach and providing the breaching party the opportunity to cure the material breach.

5.5 Upon any termination or expiration of this Collaboration Agreement, each Receiving Party shall destroy all copies of the Disclosing Party's Confidential Information.

5.6 Upon the early termination of this Agreement, Researchers shall return all unused funds to Eisai.

5.7 Upon termination of this Collaboration Agreement, the Parties agree to cooperate with each other to provide for an orderly wind-down of the Research Plan.

6. **Reports and Records**.

6.1 Researchers shall assist Eisai in preparing bi-annual reports, as well as any other such reports reasonably requested by Eisai. Eisai has sole discretion as to reporting the structural identity of its compounds (e.g., from its libraries or otherwise).

6.2 The Researchers agree to maintain adequate accounting records, as well as related evidences, documents, and materials for the Research Plan. Each Party acknowledges and agrees that its respective books and records for the Research Plan will be made available for by Eisai or its designees at reasonable times.

7. **Intellectual Property**.

7.1 Each Party will retain all rights in and to its Background Intellectual Property, Confidential Information and Intellectual Property Improvements. Each Party grants to the other Party a fully paid, non-exclusive, worldwide, royalty-free license to use

its Background Intellectual Property, Confidential Information and Intellectual Property Improvements solely to complete the Research Plan. Each Party acknowledges and agrees that neither it nor its employees or agents will acquire any rights of any kind whatsoever in any other Party's Background Intellectual Property, Confidential Information or Intellectual Property Improvements as a result of the performance of the Research Plan.

7.2 **Eisai Intellectual Property Improvements and Eisai Material Intellectual Property**. Each Party acknowledges and agrees that any Eisai Background Intellectual Property which is improved, modified or developed as a result of the Parties' performance of the Research Plan (each, a "**Eisai Intellectual Property Improvement**"), whether patentable or not, to the extent that such improvement, modification or development does not contain (i) the Confidential Information or Background Intellectual Property of another Party, (ii) constitutes a UNLP Intellectual Property Improvement, or (iii) constitutes a UNSAM Intellectual Property Improvement, shall be and remain the sole and exclusive property of Eisai.

Eisai shall solely own all Intellectual Property relating to the Material ("**Eisai Material Intellectual Property**"). For the sake of clarity, Eisai Material Intellectual Property shall include any and all forms of the Material, such as (i) pharmaceutically acceptable salts, esters, solvates, metabolites, isomers, polymorphs, or pro-drugs; (ii) any formulation or combination which contains or incorporates the Material or an above-mentioned form of the Material; (iii) any dosage or dosing regimen; (iv) any new use of the Material; or (v) any subject selection biomarker, endpoint or method; any efficacy biomarker, endpoint, or method; or any other diagnostic reagent or method. For the sake of further clarity, Eisai Material Intellectual Property shall not include new compounds jointly conceived or created by Eisai and another Party (or among Eisai and all Parties) under this Collaboration Agreement.

The Parties further agree to assign and hereby assign all rights to any Eisai Intellectual Property Improvement or Eisai Material Intellectual Property that are necessary to effect Eisai's ownership of such Eisai Intellectual Property Improvement or Eisai Material Intellectual Property.

7.3 **UNLP Intellectual Property Improvements**. Each Party acknowledges and agrees that any UNLP Background Intellectual Property which is improved, modified or developed by a party in the performance of the Research Plan (each, a "**UNLP Intellectual Property Improvement**"), whether patentable or not to the extent that such improvement, modification or development does not contain (i) the Confidential Information or Background Intellectual Property of another Party, (ii) constitutes an Eisai Intellectual Property Improvement or Eisai Material Intellectual Property, or (iii) constitutes a UNSAM Intellectual Property Improvement, shall be and remain the sole and exclusive property of UNLP.

7.4 **UNSAM Intellectual Property Improvements**. Each Party acknowledges and agrees that any UNSAM Background Intellectual Property which is improved, modified or developed by a party in the performance of the Research Plan (each, a "**UNSAM Intellectual Property Improvement**"), whether patentable or not to the extent that such improvement, modification or development does not contain (i) the

Confidential Information or Background Intellectual Property of another Party, (ii) constitutes an Eisai Intellectual Property Improvement or Eisai Material Intellectual Property, or (iii) constitutes a UNLP Intellectual Property Improvement, shall be and remain the sole and exclusive property of UNSAM.

7.5 **Joint Intellectual Property**. Any Intellectual Property conceived or reduced to practice under this Collaboration Agreement and in accordance with the Research Plan that is not (i) Eisai Material Intellectual Property or Eisai Intellectual Property Improvements, (ii) UNSAM Intellectual Property Improvement, or (iii) UNLP Intellectual Property Improvement shall be deemed "**Joint Intellectual Property**". Inventorship of any Joint Intellectual Property shall be determined in accordance with United States patent law by a United States law firm selected by Eisai. The Parties agree that any Joint Intellectual Property made hereunder shall be jointly owned. The Parties further agree to assign and hereby assign all rights to any Joint Intellectual Property that are necessary to effect joint ownership of such Joint Intellectual Property. The Parties will not prepare or file patent applications on any Joint Intellectual Property made hereunder without prior mutual written agreement.

7.6 **License**. During and after the Term of this Collaboration Agreement, the Parties will cooperate fully in obtaining proprietary protection for any patentable Joint Intellectual Property, including, but not limited to Patent Rights, at Eisai's cost and expense, and the Parties will execute and deliver all requested applications, assignments and other documents, and take such other measures as Eisai may reasonably request, in order to perfect and enforce all rights in the Joint Intellectual Property. Notwithstanding the prior sentence, Eisai is not obligated to continue pursuing, filing, prosecuting or maintaining any patent applications or patents in any country. However, Eisai will give the Researchers at least forty-five (45) days' notice of any jointly owned patent applications or patents Eisai no longer wants to pursue, file, prosecute or maintain, to allow the Researchers sufficient time to continue pursuing, filing, prosecuting or maintaining such patent applications or patents at its own expense. Each Party represents and warrants that it is free to assign its interest in Joint Intellectual Property. Each Party will promptly disclose all Joint Intellectual Property to the other Parties in writing. UNSAM and UNLP, as applicable, grant to Eisai a perpetual, non- exclusive, worldwide, fully paid, royalty free, license to UNLP's and UNSAM's interest in any Joint Intellectual Property for internal research and development purposes. UNLP and UNSAM also grant to Eisai an exclusive option to obtain an exclusive, royalty-bearing worldwide license, with the right to sublicense, any Joint Intellectual Property in order to develop, make, have made, use, sell or commercialize any product. Such option shall be exercisable within sixty (60) days of the date of filing of any jointly owned patent application. Upon exercise of the option by Eisai in writing, the Parties shall negotiate in good faith the commercially reasonable terms of the license to Eisai. Once exercised, the option shall expire in six (6) months, extendable by mutual agreement of the Parties. In the event that Eisai does not exercise its option before expiration of the option period or in the event that the Parties fail to enter into a license agreement during the option period or during such extension of time as the Parties may mutually agree, then nevertheless Eisai shall retain the non-exclusive royalty-free license to any and all of the rights of UNLP and UNSAM in and to such Joint Intellectual Property.

8. **Confidential Information; Publications**.

8.1 **Confidentiality and Proprietary Information**.

(a) Each Party (the "**Receiving Party**") agrees to treat any Confidential Information of the other Party (the "**Disclosing Party**") as confidential and the exclusive property of the Disclosing Party. The Disclosing Party shall endeavor to mark tangible Confidential Information provided to Receiving Party as "Confidential", provided that Receiving Party confirms and agrees that Disclosing Party's failure to identify any information as Confidential Information shall not constitute a designation of non-confidentiality when the confidential nature of the information is apparent from the subject matter, the circumstances of disclosure or when the information is such that a reasonable person would consider it to be proprietary or confidential.

(b) The Receiving Party agrees not to disclose any of the prior Confidential Information of the Disclosing Party without first obtaining the written consent of the Disclosing Party. The Receiving Party agrees that it will use any such Confidential Information of the Disclosing Party only for purposes of performing the Research Plan or any obligations under this Agreement and for no other purpose without the prior written consent of the Disclosing Party. The Parties further agree to take all practicable steps to ensure that such Confidential Information will not be used by its directors, officers or employees except for the performance of such Party's obligations under this Agreement and any Confidential Information will be kept fully private and confidential by them. Such Receiving Party's obligations of confidentiality shall survive any expiration or termination of this Agreement for a period of ten (10) years after the completion of the Research Plan.

(c) The above provisions of confidentiality shall not apply to any Confidential Information that the Receiving Party is able to demonstrate by competent and reliable evidence: (i) was lawfully in the Receiving Party's possession prior to receipt from Disclosing Party; or (ii) was in the public domain at the time of receipt from the Disclosing Party; or (iii) becomes part of the public domain through no fault of the Receiving Party, its directors, officers or employees; or (iv) is lawfully received by the Receiving Party from some third party having a right of further disclosure and such third party did not obtain the information from the Receiving Party; or (v) is independently developed by or on behalf of the Receiving Party outside of this Agreement without the use of, or reference to, any Confidential Information as defined by this Agreement. Additionally, and notwithstanding anything to the contrary in this Section 7, the Receiving Party may disclose the Confidential Information of the Disclosing Party to the extent required by applicable law or regulation, *provided* that the Receiving Party gives the Disclosing Party prompt, prior written notice of the required disclosure and sufficient opportunity to object to such use or disclosure or to request confidential treatment of the Confidential Information, at the Disclosing Party's own expense.

(d) The Researchers shall not publish any articles, or make any presentations

relating to the Research Plan or referring to Eisai Confidential Information or any Intellectual Property it does not own outright or results generated as part of the Research Plan, in whole or in part, without the prior written consent of Eisai.

(e) Neither anything herein contained nor any delivery of Confidential Information by either Party to the other shall be deemed to grant to the Receiving Party any rights or licenses under any patent applications or patents or to any know-how, technology or inventions of the Disclosing Party.

8.2 **Protection of Nonpublic Personal Information**.

(a) The Parties acknowledge that, to the extent it is in the possession of, may receive or gain access to Nonpublic Personal Information or ("**NPI**") each Party will comply with applicable data privacy laws and regulations and will maintain adequate administrative, technical, and physical safeguards to: (a) ensure the security and confidentiality of the information; (b) protect against any anticipated threats or hazards to the security or integrity of the information; (c) protect against unauthorized access to or use of the information that could result in substantial harm to each Party or to any individual; and (d) ensure the proper disposal of NPI as required by applicable laws and regulations. Each Party shall ensure that the above-referenced safeguards comply with the requirements of all applicable data security and encryption-related laws and regulations.

(b) As used herein, NPI shall mean information that is not publicly available and that, in itself or as part of a unique combination of data or information, identifies or could be used to identify an individual, whether by unique descriptors and/or identifiers, including but not limited to social security numbers, health plan/insurance policy numbers, financial account (including credit card/debit card) numbers, driver's license numbers, and/or any other unique identifying numbers, characteristics, or codes.

(a) Eisai may take reasonable and appropriate steps to help ensure that the Researchers process NPI in a manner consistent with Eisai's obligations under Data Privacy Laws. The Researchers shall notify Eisai if it makes a determination that it can no longer meet its obligations under this Agreement and Data Privacy Laws. Eisai may, upon reasonable notice to the Researchers, take reasonable and appropriate steps to stop and remediate unauthorized Processing of NPI.

8.3 **Right of Publication/Name Use**.

(a) The Researchers shall not make any presentation, publication, or submit any manuscript for publication without the prior written approval from Eisai, which shall not be unreasonably withheld. Any Eisai approved publication shall be a collaborative effort between all Parties and shall be consistent with ICMJE ethical guidelines. The Parties shall mutually decide which Party will draft any such publication. Prior to submitting or presenting a publication to

a publisher, reviewer, or third party, the initial drafter shall provide to the other Party a copy of all such manuscripts and materials, each Party shall have forty five (45) days from receipt of such publication to review and comment.

(b) Construction of the list of the publication co-authors and the specific order of those authors shall be congruent with common practice in publication of scientific findings. Additionally, any publication shall acknowledge the contributions of GHIT and MMV.

(c) Upon request, the publishing Party shall remove any Confidential Information of the requesting Party prior to submitting or presenting the publication, and the Researchers further shall, upon request, delay publication or presentation for a period of up to ninety (90) days to allow the requesting Party to protect its interests in any inventions described in any such materials.

(d) The Parties will make the safety and efficacy results of the Research Project available to the public. The Parties will seek prompt publication of any such data and results generated from the Research Project in a peer-reviewed journal or trade publication, as applicable. The Parties will cite all actual or pending publications in the progress reports that are submitted to Eisai .

(e) No Party to this Agreement shall use any other Party's (or such Party's Affiliates) names, trade names, service marks, trademarks or logos for any purpose, including in connection with any advertising or promotion of any product or service without the prior written permission of Eisai. The Parties agree that they will not disclose the terms of this Agreement to an outside party without the prior written consent of Eisai. For the sake of clarity, an "outside party" does not include the parties to the Investment Agreement. For the purpose of meeting reporting obligations, the Parties are specifically authorized to publicly disclose the following information about the Agreement if required by applicable law and regulations: a summary specifying the parties, date of signature, objective, and date of expiration. Notwithstanding the immediately preceding sentence, the information disclosed shall be limited to the minimum information necessary required to satisfy each obligation and any objective of the Research Project disclosed shall include only the Research Project related information that is already disclosed on ghitfund.org. Additionally, for the avoidance of doubt, the Researchers shall not publicly disclose the names of GHIT or MMV without Eisai's prior written approval.

9. **Representations and Certifications**.

9.1 Eisai represents and warrants that it is a duly formed and validly existing entity under the laws of Japan.

9.2 UNSAM represents and warrants that it is a duly formed and validly existing entity under the laws of Argentina.

9.3 UNLP represents and warrants that it is a duly formed and validly existing entity under the laws of Argentina.

9.4 The Parties represent and warrant that:

(a) They have all power and authority (corporate or otherwise) to execute and deliver this Collaboration Agreement and to perform its obligations hereunder. The Parties execution and delivery of, and performance under, this Collaboration Agreement have been duly and validly authorized by all necessary action.

(b) Upon execution and delivery of this Collaboration Agreement, this Collaboration Agreement shall constitute a legal, valid and binding agreement of each of the Parties, enforceable in accordance with its terms, except to the extent enforceability may be affected by applicable bankruptcy, reorganization, insolvency and moratorium laws and other laws applicable generally to creditors' rights and debtors' remedies from time to time in effect.

(c) Neither the execution and delivery of this Collaboration Agreement nor to the best of its knowledge, after undertaking reasonable due diligence, no Party's performance of its obligations hereunder will violate or breach, or otherwise constitute or give rise to a default under, nor conflict with any material contract, commitment or other obligation to which said Party is a party, or any judgment, order, decree, rule or regulation of any court or governmental agency to which said Party is subject.

(d) Each Party is aware of and understands that there are anti-bribery and anti-corruption statutes (including, but not limited to, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.K. Bribery Act 2010 and Article 18 of the Unfair Competition Prevention Act of Japan) to which each Party is subject that prohibit the payment or offering, giving, promising to give, or authorizing the giving of, directly or indirectly, anything of value to a Government Official (as defined herein), or any relative, business associate or employee thereof, for the purpose of obtaining or retaining any business under this Collaboration Agreement or inducing or influencing any governmental act or decision. Each Party hereby agrees to refrain from any activity in connection with this Agreement that would constitute a violation by any Party of such anti-bribery and anti-corruption statutes, including sharing, directly or indirectly, any of the funds paid to each Party under this Agreement with a Government Official. Similarly, no Party shall, directly or indirectly, request, accept, or agree to accept any item of value that could be seen as an attempt to compromise its independence of judgment or improperly influence a business decision. "**Government Official**", broadly defined includes without limitations, any officer (elected or appointed) or employee of a government or public organization or institution, or a department, agency or instrumentality of any of the foregoing, any official of a political party or a candidate for political office, or anyone otherwise categorized as a Government Official under applicable laws and regulations.

(e) Upon request, or should any Party ever become the subject of an audit or investigation by a governmental authority, including under any anti-boycott regulations, anti-bribery legislation, or related export legislation, each Party agrees to cooperate fully with the requesting Party in connection with such investigation and to provide such information and records to the requesting Party with respect to that Party's activities under this Agreement as may be reasonably requested by the requesting Party.

(g) This Agreement may be terminated in the event any Party breaches any of the above representations and warranties or if any Party learns that improper payments are being or have been made to Government Officials.

10. **Indemnification and Limitation of Liability**.

10.1 **Indemnification**.

(a) **UNLP Indemnity**. UNLP shall indemnify, defend and hold harmless Eisai and UNSAM and their respective employees and agents from and against any and all damages, liabilities, losses, fines, penalties, settlement amounts, costs and expenses of any kind or nature whatsoever, including, without limitation, reasonable attorney's fees, expert witnesses and court costs, incurred in connection with any claim, demand, action, proceeding, investigation or hearing brought by a third party (collectively, a "**Claim**") arising out of, resulting from, or in connection with (a) the acts or omissions, actual or alleged, of UNLP or any of their respective directors, statutory auditors, officers, agents, employees, contractors or subcontractors with respect to any activities involved in the Research Plan, such as clinical trials involving human subjects, post-approval studies, field trials involving genetically modified organisms, experimental medicine and the provision of medical/health services, (b) any breach of this Collaboration Agreement by UNLP, (c) any negligence or willful misconduct by UNLP or any of their directors, statutory auditors, officers, agents, employees, contractors or subcontractors with respect to the Research Plan, (d) the marketing, distribution, sale, licensing or use of any products developed under the Research Plan, or (e) any other activities of UNLP related to the Research Plan, except, in each of the foregoing clauses (b) through (e), to the extent that any such claim, loss, cost or damages is attributable to any gross negligence or willful misconduct by Eisai or UNSAM.

(b) **UNSAM Indemnity**. UNSAM shall indemnify, defend and hold harmless Eisai and UNLP and their respective employees and agents from and against any and all Claims arising out of, resulting from, or in connection with (a) the acts or omissions, actual or alleged, of UNSAM or any of their respective directors, statutory auditors, officers, agents, employees, contractors or subcontractors with respect to any activities involved in the Research Plan, such as clinical trials involving human subjects, post-approval studies, field trials involving genetically modified organisms, experimental medicine and the provision of medical/health services, (b) any breach of this Collaboration Agreement by UNSAM, (c) any negligence or willful misconduct by UNSAM or any of their directors, statutory auditors, officers, agents,

employees, contractors or subcontractors with respect to the Research Plan, (d) the marketing, distribution, sale, licensing or use of any products developed under the Research Plan, or (e) any other activities of UNSAM related to the Research Plan, except, in each of the foregoing clauses (b) through (e), to the extent that any such claim, loss, cost or damages is attributable to any gross negligence or willful misconduct by Eisai or UNLP.

(c) **Eisai Indemnity**. Eisai shall indemnify, defend and hold harmless UNLP and UNSAM and their respective employees and agents from and against any and all Claims arising out of, resulting from, or in connection with (a) the acts or omissions, actual or alleged, of Eisai or any of their respective directors, statutory auditors, officers, agents, employees, contractors or subcontractors with respect to any activities involved in the Research Plan, such as clinical trials involving human subjects, post-approval studies, field trials involving genetically modified organisms, experimental medicine and the provision of medical/health services, (b) any breach of this Collaboration Agreement by Eisai, (c) any negligence or willful misconduct by Eisai or any of their directors, statutory auditors, officers, agents, employees, contractors or subcontractors with respect to the Research Plan, (d) the marketing, distribution, sale, licensing or use of any products developed under the Research Plan, or (e) any other activities of Eisai related to the Research Plan, except, in each of the foregoing clauses (b) through (e), to the extent that any such claim, loss, cost or damages is attributable to any gross negligence or willful misconduct by UNLP or UNSAM.

(d) **Claim Defense**. Any Party obligated to provide indemnification hereunder with respect to a Claim shall be entitled to control the defense of the Claim, *provided* that the indemnifying party shall act reasonably and in good faith with respect to all matters relating to the Claim. The indemnified party or parties shall reasonably cooperate in the investigation, defense and settlement of a Claim for which indemnification is sought hereunder and shall provide prompt notice of the Claim to the indemnifying party. The indemnifying party shall not enter into any settlement without the prior written consent of the indemnified party or parties, such consent to not be unreasonably withheld or delayed. At any time by providing written notice to the indemnifying party, the indemnified party or parties shall have the right to waive any and all indemnification obligations and retain separate legal counsel at its own expense.

(e) Each Party will maintain insurance coverage sufficient to cover the activities, risks and potential omissions of the Research Plan in accordance with generally accepted industry standards and as required by law. Each Party will ensure that their subcontractors will maintain insurance coverage consistent with this Collaboration Agreement.

(f) **Limited Liability**. IN NO EVENT SHALL ANY PARTY HAVE ANY LIABILITY TO THE OTHER PARTIES OR TO THIRD PARTIES FOR ANY INDIRECT, INCIDENTAL, SPECIAL, CONSEQUENTIAL OR PUNITIVE DAMAGES, EVEN IF SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY THEREOF. THE ALLOCATIONS OF LIABILITY

IN THIS SECTION REPRESENT THE AGREED AND BARGAINED-FOR UNDERSTANDING OF THE PARTIES WITH RESPECT TO ALLOCATION OF RISKS INHERENT IN THEIR RELATIONSHIP.

11. **Notices and Communications**.

11.1 Except as expressly provided otherwise herein, all notices, statements, requests and demands given to or made upon any Party hereto in accordance with the provisions of this Agreement shall be in writing and shall be deemed to have been given or made when delivered by hand or by facsimile (with the hard copy sent by registered or certified mail, return receipt requested, or by Federal Express or similar overnight courier), in each case addressed as below:

If to UNLP:

Facultad de Ciencias Exactas
UNLP
Calles 47 y 115 s/n
La Plata (B1900ADD)
Buenos Aires, Argentina

Attn: Prof. Mauricio F. Erben (dean)
Email: decanato@exactas.unlp.edu.ar

If to UNSAM:
Edificio de Gobierno- Campus Miguelete
Av. 25 de Mayo 1405
San Martín (1650), Buenos Aires
Argentina

Attn: Julio Bayona, PhD
e-mail: secretaria_idi@unsam.edu.ar

If to Eisai:

4-6-10 Koishikawa
Bunkyo-ku
Tokyo 112-8088
Japan
Attn: Legal Counsel

With a copy to:

Eisai Inc.
200 Metro Boulevard
Nutley, NJ 07110
Attn: Fabian Gusovsky, Ph.D. Email:
Fabian_Gusovsky@eisai.com

Any of the Parties may designate a different contact person or address as they may

choose to do so by the issuance of a formal written notice in accordance herewith.

12. **General Provisions**.

12.1 This Collaboration Agreement together with its exhibits sets forth the entire understanding between the Parties hereto and supersedes all prior agreements, arrangements and communications, whether oral or written, with respect to the subject matter hereof. No other agreements, representations, warranties or other matters, whether oral or written, shall be deemed to bind the parties hereto with respect to the subject matter hereof.

12.2 This Agreement may be executed in a unique electronic document.

12.3 The delay or failure by any Party to exercise or enforce any of its rights under this Collaboration Agreement shall not constitute or be deemed a waiver of that Party's right thereafter to enforce those rights, nor shall any single or partial exercise of any such right preclude any other or further exercise thereof or the exercise of any other right.

12.4 No Party shall not assign or transfer any rights or obligations under this Collaboration Agreement. Each Party has the right to select a subcontractor to assist with the Research Plan, provided that such Party shall (a) ensure such subcontractor's compliance with the terms of this Collaboration Agreement and (b) remain liable and responsible to the other Parties hereto for such subcontractor's performance.

12.5 In connection with this Collaboration Agreement, each Party is an independent contractor and as such will not have any authority to bind or commit the other. Nothing herein shall be deemed or construed to create a joint venture, partnership, fiduciary or agency relationship between the parties for any purpose.

12.6 If any term or provision of this Collaboration Agreement is found by a court of competent jurisdiction to be invalid, illegal or otherwise unenforceable, the same shall not affect the other terms or provisions hereof or the whole of this Collaboration Agreement, but such term or provision shall be deemed modified to the extent necessary in the court's opinion to render such term or provision enforceable, and the rights and obligations of the parties shall be construed and enforced accordingly, preserving to the fullest permissible extent the intent and agreements of the parties herein set forth.

12.7 The terms of this Collaboration Agreement that contain obligations or rights that extend beyond the completion of the Research Plan shall survive termination or completion of this Collaboration Agreement.

12.8 This Agreement shall be governed by and construed in accordance with the laws of Japan, and the Parties agree that, in the event of a dispute arising out of the operation and performance of this Collaboration Agreement, they will exercise their best efforts to resolve said dispute prior to their availing themselves of their remedies at law or in equity.

[Signature page follows]

IN WITNESS WHEREOF, the Parties have caused their duly authorized representatives to execute this Agreement as of the Effective Date.

UNIVERSIDAD NACIONAL DE LA PLATA

By: _____
Name: ERBEN Mauricio Federico
Title: _____
Date: _____

Firmado digitalmente por ERBEN Mauricio Federico
Fecha: 2025.04.08 18:23:20 -03'00'

VARELA Andrea Mariana

Firmado digitalmente por VARELA Andrea Mariana
Fecha: 2025.04.09 16:18:11 -03'00'

EISAI CO., LTD.

署名者:
B2A8D8951C0A40D...

By: _____
Name: Kappei Tsukahara
Title: Head of Global Health
Date: 2025年4月14日

UNIVERSIDAD NACIONAL DE SAN MARTIN

By: GRECO Carlos
Name: _____
Title: _____
Date: _____

Firmado digitalmente por GRECO Carlos
Fecha: 2025.02.28 12:54:08 -03'00'

FUNDACIÓN CIENCIAS EXACTAS

By: CAPPARELLI Alberto Luis
Name: _____
Title: _____
Date: _____

Firmado digitalmente por CAPPARELLI Alberto Luis
Fecha: 2025.04.08 13:32:51 -03'00'

EXHIBIT A

RESEARCH PLAN

(see attached)

EXHIBIT B

BUDGET

(see attached)

GHIT Fund Drug Discovery Screening Platform
Reference Number: GHIT-RFP-Screening-2024-001
Contact Form

Please fill out the following information and submit it by e-mail to RFPResponse@ghitfund.org (please include in the subject the following: "Potential Screening Platform 2024-001"). GHIT Fund Management Team will then perform an initial partnership and scope eligibility assessment. Questions specific to this Screening Platform can only be answered with the submission of this information.

Eligible applicants will receive an email with GHIT Fund Budget template as an attachment and its submission deadline – please complete the Budget template and submit it by the indicated deadline to RFPResponse@ghitfund.org

	Partner 1	Partner 2
Organization Name	Eisai Co. Ltd.	Choose one PDP: ☐ DNDi ☐ TB Alliance ☒ MMV
Organization Type (e.g., PDP, pharma company, academic institution)	Pharma company	PDP
Organization Status	☒ Japanese	☒ Non-Japanese
Name of Contact Person *(Nominate one person from each partner as the main contact with the GHIT Fund)*	Julian Peat ☒ Main Contact Point	Benoît Laleu ☒ Main Contact Point
Designated Development Partner *(Nominate one partner)*	☐	☒
Title	Dr	Dr
E-mail Address	julian_peat@eisai.com	laleub@mmv.org
Direct Phone No.	+1 8882742378	
Cell Phone No.	+1 9788098565	+41 763522086
Disease of interest *(check all that apply)*	☐ Tuberculosis ☐ Malaria ☐ Chagas disease ☐ Leishmaniasis ☐ Emerging and Re-Emerging Infectious Diseases* *Please specify □ Ebola virus (*Filoviridae*) □ Marburg virus (*Filoviridae*) □ Lassa fever (*Arenaviridae*) □ Nipah virus (*Paramyxoviridae*) □ Henipa virus (*Paramyxoviridae*)	

	□ Rift Valley fever (*Bunyaviridae*) □ Zika (*Flaviviridae*) ☒ Chikungunya (*Togaviridae*) □ Rabies (*Rhabdoviridae*) □ Others

Please provide the total amount needed to fund your project. (Note: If your application is eligible, the GHIT Management Team will send an Excel template shortly and ask the partnership to submit a detailed Budget plan describing a detailed budget plan associated with each activity/milestone and the amount of in-kind contribution, if any). [Please insert budget in Japanese Yen]._

Total requested budget:
Direct costs: $131,000 / ¥20,960,000
Indirect costs: $18,340 / ¥2,934,400
Total costs: $149,340 / ¥23,894,400
Conversion to Japanese Yen assumes $1 = ¥160

Please describe the main objectives and activities/milestones of your project and write an estimated timeline (month/year) of the objectives/milestone and the duration of your project (Note: The start month/year should be at least eight weeks after the submission of the Contact Form). In addition, please describe the partnerships' future research plan in case there are positive findings from this Screening program.

Alphaviruses, belonging to the *Togaviridae* family, are small, enveloped RNA viruses with a single-stranded, positive-sense RNA genome. They are typically transmitted by arthropods and are known to cause diseases in both humans and animals[1]. New World alphaviruses, such as Venezuelan and Western equine encephalitis viruses (VEEV and WEEV), are commonly associated with encephalitic diseases[1]. Conversely, Old World alphaviruses like Chikungunya virus (CHIKV) and Mayaro virus (MAYV) generally cause arthritogenic febrile illness[1]. Acute chikungunya manifests with high fever, arthralgia, headache, and nausea. Approximately 51% of symptomatic individuals experience chronic sequelae, including persistent arthralgia, myalgia, chronic arthritic disability, and increased mortality associated with the disease[2].

The reemergence of CHIKV in recent decades has caused major outbreaks across many regions, particularly in Latin America, the Caribbean, and South Asia[3]. This underscores the significant threat alphaviruses currently pose to human health. In 2018, CHIKV was added to the World Health Organization's (WHO) shortlist for priority research and development as a neglected tropical disease due to the lack of an approved vaccine and the potential for chronic dysfunction. With no approved targeted drug treatments, medical care primarily involves supportive measures, typically prescribing non-steroidal anti-inflammatory drugs to alleviate symptoms. Although vaccines against CHIKV have recently been approved[4], there is limited knowledge about the duration of their protection and their efficacy in preventing outbreaks. Therefore, there is an urgent need for the development of new therapeutics for CHIKV and related alphaviruses.

Here, we propose computationally-enhanced screening for novel compounds active against CHIKV. This approach leverages advanced machine-learning models to cost-effectively screen a large Eisai compound library, followed by focused experimental screening using established assays in Argentina. The collaboration leverages the synergy of artificial intelligence, screening capabilities and drug development expertise between a pharmaceutical company, PDP and academic investigators in a CHIKV-endemic country.

Project Objective: Identify novel compounds against CHIKV using AI-enhanced screening of Eisai's library
Overall Timeline: October 2024 to July 2025 (10 months)

Milestone 1: Identification of Primary Hits
Timeline: October 2024 to March 2025 (6 months)

The primary screen will take an innovative two-step approach to maximize the compound space assessed for potential activity against CHIKV.

Activity 1A: AI-based screening of Eisai library (>200,000 compounds)

The large Eisai compound library will be computationally screened using a phenotypic machine learning model developed by Prof. Alan Talevi's team at the Universidad Nacional de La Plata (UNLP), Argentina. The model will be generated based on selective ensemble learning of linear classifiers. UNLP has previously demonstrated success with this approach [5–7], including promising results in the GHIT-funded T2020-154 project for Chagas Disease. We will complement this approach with supervised clustering based on an adaptation of the in-house iRaPCA algorithm[8]. High-quality data will be used for the modeling procedures, including in-house data from more than 400 compounds already subjected to phenotypic screening at Universidad Nacional de San Martín (UNSaM)[9], and manually curated data collected from literature. We will complement this *in silico* phenotypic screening with models aimed at possible pharmacological targets, in order to provide initial clues regarding the possible mechanism of action of the *in silico* hits. Based on the information available, we will make use of a combination of machine learning and structure-based models for CHIKV nsP1 methyltransferase and nsP2 protease, as well as structure-based methods for the viral polymerase nsP4 and envelope proteins. The machine learning models are now being developed at-risk by UNLP, so that the team will be able to initiate this computational screening immediately upon receipt of GHIT funding.

Activity 1B: Primary experimental screening of top 9,000 computational hits

From this computational screen, the top 9,000 compounds will be selected and provided by Eisai for primary experimental screening by Prof. Diego Alvarez's team at UNSaM, Argentina. Prof Alvarez has extensive experience working with alphaviruses and a well-established CHIKV screening assay [9–12].
Primary screens will be performed in a 96-well plate format using a 1X format at a single compound concentration (10 μM), and a fully infectious recombinant virus expressing the fluorescent protein ZsGreen as a reporter to infect cells. The readouts that will be obtained at 18 hours post-treatment include: 1) automated numbering of fluorescent foci of infection, and 2) crystal violet staining as surrogate to initially assess compound effect on cell viability.
Screening actives (primary hits) will be selected based on higher than 50% reduction of foci counts and less than 30% reduction in absorbance of crystal violet staining compared to vehicle treated controls.

Milestone 2: Identification and Further Profiling of Confirmed Actives (planning for 5-10 Confirmed Actives)
Timeline: April 2025 to July 2025 (4 months)

Activity 2A: Secondary screening of prioritized primary hits

Approximately 50 primary hits from the activities outlined in Milestone 1 will be selected for activity confirmation studies. Additional compound will be supplied by Eisai to UNSaM to conduct these assays. Dose response curves (EC_{50}) will be generated for selected compounds in the CHIKV assay. The cytotoxicity profile (CC_{50}) will also be assessed with the MTS assay.

Activity 2B: Profiling of confirmed actives against additional alphaviruses

Eisai and MMV will prioritize up to 5-10 confirmed actives for further profiling. Preference will be given to compounds belonging to clusters of structurally related chemotypes.

To assess further their potential for broad spectrum activity within a virus family, these confirmed actives will be profiled at UNSaM against other alphaviruses: the Old-World Ross River and Mayaro viruses and New World Venezuelan Equine Encephalitis Virus (VEEV). The confirmed hits will also be tested against live CHIKV of the epidemic Indian Ocean and Caribbean lineages.
To assess specificity for the alphavirus genus, these confirmed actives will also be tested at UNSaM against SARS-CoV2 and mosquito-borne flaviviruses. UNSaM have already established assays to test antiviral activity against SARS-CoV-2,[13-15] and have extensive expertise in the manipulation of flaviviruses, including dengue and Zika viruses.[16-19]

The hit series meeting MMV and GHIT criteria for further development (hits with confirmed EC_{50} <5 μM vs live viruses and selectivity index ($SI = CC_{50}/EC_{50}$) ≥10, progressable chemotypes) will form the basis of a future GHIT HTLP proposal. The project partners are engaged and well-positioned to progress the identified hits to this next stage. In addition, the project team has already had productive discussions with the team of Dr. Mariela Bollini at the Centro de Innovación en Bionanociencias (CIBION) in Argentina, which has medicinal chemistry and physicochemical profiling capabilities that would complement the existing partners' abilities to effectively execute a hit-to-lead program.

References

1. Levi, L. I. & Vignuzzi, M. Arthritogenic Alphaviruses: A Worldwide Emerging Threat? *Microorganisms* **7**, (2019).
2. Kang, H. *et al.* Chikungunya seroprevalence, force of infection, and prevalence of chronic disability after infection in endemic and epidemic settings: a systematic review, meta-analysis, and modelling study. *Lancet Infect Dis* **24**, 488–503 (2024).
3. Pegado, R., Mendes Neto, N. N., Pacheco-Barrios, K. & Fregni, F. Chikungunya crisis in the Americas: a comprehensive call for research and innovation. *The Lancet Regional Health - Americas* **34**, (2024).
4. Ng, L. F. P. & Rénia, L. Live-attenuated chikungunya virus vaccine. *Cell* **187**, 813-813.e1 (2024).
5. Alberca, L. N., Chuguransky, S. R., Álvarez, C. L., Talevi, A. & Salas-Sarduy, E. In silico Guided Drug Repurposing: Discovery of New Competitive and Non-competitive Inhibitors of Falcipain-2. *Front Chem* **7**, 467991 (2019).
6. Ruatta, S. M. *et al.* Garbage in, garbage out: how reliable training data improved a virtual screening approach against SARS-CoV-2 MPro. *Front Pharmacol* **14**, 1193282 (2023).
7. Bélgamo, J. A. *et al.* Application of target repositioning and in silico screening to exploit fatty acid binding proteins (FABPs) from Echinococcus multilocularis as possible drug targets. *J Comput Aided Mol Des* **34**, 1275–1288 (2020).
8. Gantner, M. E. *et al.* Identification of New Carbonic Anhydrase VII Inhibitors by Structure-Based Virtual Screening. *J Chem Inf Model* **62**, 4760–4770 (2022).
9. Castro, E. F. & Álvarez, D. E. New highly selective antivirals for Chikungunya Virus identified from the screening of a drug-like compound library. *bioRxiv* 2024.05.17.594707 (2024) doi:10.1101/2024.05.17.594707.
10. Battini, L., Fidalgo, D. M., Álvarez, D. E. & Bollini, M. Discovery of a Potent and Selective Chikungunya Virus Envelope Protein Inhibitor through Computer-Aided Drug Design. *ACS Infect Dis* **7**, 1503–1518 (2021).
11. Bardossy, E. S., Volpe, S., Alvarez, D. E. & Filomatori, C. V. A conserved Y-shaped RNA structure in the 3'UTR of chikungunya virus genome as a host-specialized element that modulates viral replication and evolution. *PLoS Pathog* **19**, (2023).
12. Merwaiss, F. *et al.* Chikungunya Virus Replication Rate Determines the Capacity of Crossing Tissue Barriers in Mosquitoes. *J Virol* **95**, (2021).
13. Coria LM, Saposnik LM, Pueblas Castro C, Castro EF, Bruno LA, Stone WB, Pérez PS, Darriba ML, Chemes LB, Alcain J, Mazzitelli I, Varese A, Salvatori M, Auguste AJ, Álvarez DE, Pasquevich KA, Cassataro J. A Novel Bacterial Protease Inhibitor Adjuvant in RBD-Based COVID-19 Vaccine Formulations Containing Alum Increases Neutralizing Antibodies, Specific Germinal Center B Cells and Confers Protection Against SARS-CoV-2 Infection in Mice. Front Immunol. 2022 Feb 28;13:844837. doi: 10.3389/fimmu.2022.844837.
14. Castro EF, Acosta J, Moriena L, Rios Medrano M, Tejerina Cibello M, Codino E, Taborda MÁ, Álvarez DE, Cavatorta AL. Longitudinal Follow-Up of the Immunity to SARS-CoV-2 in Health Care Workers in Argentina: Persistence of Humoral Response and Neutralizing Capacity after

Sputnik V Vaccination. mSphere. 2023 Jun 22;8(3):e0066222. doi: 10.1128/msphere.00662-22.
15. Coria LM, Rodriguez JM, Demaria A, Bruno LA, Medrano MR, Castro CP, Castro EF, Del Priore SA, Hernando Insua AC, Kaufmann IG, Saposnik LM, Stone WB, Prado L, Notaro US, Amweg AN, Diaz PU, Avaro M, Ortega H, Ceballos A, Krum V, Zurvarra FM, Sidabra JE, Drehe I, Baqué JA, Li Causi M, De Nichilo AV, Payes CJ, Southard T, Vega JC, Auguste AJ, Álvarez DE, Flo JM, Pasquevich KA, Cassataro J. A Gamma-adapted subunit vaccine induces broadly neutralizing antibodies against SARS-CoV-2 variants and protects mice from infection. Nat Commun. 2024 Feb 2;15(1):997. doi: 10.1038/s41467-024-45180-8.
16. Castellano LA, McNamara RJ, Pallarés HM, Gamarnik AV, Alvarez DE, Bazzini AA. Dengue virus preferentially uses human and mosquito non-optimal codons. Mol Syst Biol. 2024 Jul 22. doi: 10.1038/s44320-024-00052-7.
17. Villordo SM, Alvarez DE, Gamarnik AV. A balance between circular and linear forms of the dengue virus genome is crucial for viral replication. RNA. 2010 Dec; 16(12):2325-35. doi: 10.1261/rna.2120410.
18. Alvarez DE, Lodeiro MF, Ludueña SJ, Pietrasanta LI, Gamarnik AV. Long-range RNA-RNA interactions circularize the dengue virus genome. J Virol. 2005 Jun; 79(11):6631-43. doi: 10.1128/JVI.79.11.6631-6643.2005.
19. Pallarés HM, *et al.* Zika virus non-coding RNAs antagonize antiviral responses by PKR-mediated translational arrest, Nucleic Acids Research, 2024, gkae507. doi: 10.1093/nar/gkae507.

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End-of-Document

	UNSAM	UNLP
Milestone 1 - direct costs	¥ 4.000.000,00	¥ 1.600.000,00
Milestone 2 - direct costs	¥ 4.960.000,00	
Indirect costs	¥ 1.254.400,00	¥ 224.000,00
TOTAL	¥ 10.214.400,00	¥ 1.824.000,00