LEO PHARMA OPEN INNOVATION AGREEMENT FOR

COMPOUND BIOACTIVITY TEST

- includes transfer of material

This Open Access agreement to test compounds for disease-relevant bioactivity ("**Agreement**") is entered into by LEO Pharma A/S, Industriparken 55, 2750 Ballerup, Denmark ("**LEO**") and the institution identified in Appendix 1 ("**Institution**") (LEO and Institution also referred to individually as "Party" and jointly as "Parties"). The Agreement is effective as of the date of the last Party to sign the Agreement ("**Effective Date**").

The Parties agree that this Agreement is beneficial to both Parties and therefore the Parties agree that no modification to the Agreement is required as the intention with the open innovation platform is to have a simple and smooth process as possible.

1 BACKGROUND

1.1 LEO is a foundation-owned pharmaceutical company focusing on dermatology and skin inflammation. LEO is interested in exploring new opportunities and ways of working with external research partners. To achieve this LEO has set out to establish a collaborative space within which LEO and Institution will be able to explore new opportunities by way of making available to each other compounds and research tools.

1.2 The aim of the Open Innovation initiative is to reduce the complexity of initiating scientific collaboration by allowing external partners easy access to test compounds for bioactivity in disease-relevant functional cell-based *in vitro* assays as provided by LEO.

1.3 LEO and Institution are interested in collaborating by means of this Agreement and then evaluating further activities. The aim of this Agreement is to facilitate the actual sharing of compounds and biological assays, while creating scientific data without any initial business constraints. Should the generated data be of interest to LEO, LEO will discuss with Institution the possibility to conduct additional analysis. Such additional analyses will be subject to Institution's written consent and certain agreed conditions

1.4 A description of the overall procedure can be found in Appendix 2 ("Procedure") highlighting key steps.

2 PROCESS OVERVIEW

2.1 Institution will provide to LEO compound sample(s) as specified in Appendix 3 of this Agreement ("**Submitted Compounds**"). The Submitted Compounds will be tested in a number of the available assays as described in Appendix 4. Such tests include (i) assessment of the Submitted Compound for biological functionality in the assays and; (ii) determination of molecular weight and degree of purity as a quality control ("**Research**"). All such testing is done for non-commercial purposes.

2.2 All Submitted Compounds provided and the testing hereof shall be subject to the terms and conditions as described in this Agreement.

2.3 Results generated from the Research ("**Research Results**") will be provided to Institution's Contact Person in a written report ("**Research Report**") in the format specified in Appendix 5 after the conclusion of the Research.

3 HOW TO SUBMIT COMPOUNDS TO LEO

3.1 As part of this Agreement, Institution agrees to provide LEO with enough quantities of Submitted Compounds and relevant information required in order for LEO to perform the Research.

3.2 Institution will in agreement with LEO appropriately package, label and ship Submitted Compounds to LEO all in accordance with applicable law.

3.3 If Submitted Compounds are transferred across borders, Institution is responsible for ensuring compliance with applicable laws and regulations regarding export of the Submitted Compound. Institution is responsible for determining the requirement for the shipment of Submitted Compounds and shall select carriers that are skilled and experienced in handling and shipping of these types of compounds. Furthermore Institution shall arrange the shipments and handle all activities in connection with import and export, including but not limited to customs clearance and payment of custom duties and other related charges. Institution accepts to assume

all risks (e.g. loss/damage to the Submitted Compounds) in connection with and is responsible for shipment (regardless means of transportation) of Submitted Compound to LEO for Research. If Submitted Compounds are lost or damaged during transit to LEO, Institution may submit additional Submitted Compounds for Research. LEO assume no liability whatsoever in relation to the submitted Compounds.

3.4 LEO will confirm receipt of Submitted Compounds by e-mail to the Contact Person identified by Institution in Appendix 1.

4 LEO USE OF SUBMITTED COMPOUNDS

4.1 The exact list of assays used for testing of Submitted Compounds may vary pending on availability and is always subject to the decision of LEO. Subject to written approval by Institution LEO reserves the right to test Submitted Compounds in assays currently being developed for but not yet included in the Open Innovation platform described in Appendix 4; nevertheless LEO will still communicate any Research Results to Institution.

4.2 LEO agrees:

4.2.1 to use Submitted Compounds only for the Research;

4.2.2 to generate data as part of the Research; summarize these in a Research Report and provide the Research Report to Institution;

4.2.3 to limit access to Submitted Compounds and Research Results to LEO employees, and agents, consultants or contractors engaged or working with LEO who are bound by relevant terms and conditions similar to this Agreement;

4.2.4 to maintain the same degree of security with respect to Submitted Compounds and data generated from Research as is maintained by LEO for its own confidential, proprietary and valuable material;

4.2.5 that the provision of Submitted Compounds to LEO does not constitute a representation on behalf of Institution and that the possession or use of Submitted Compounds will not infringe any patent or proprietary rights of any third party;

4.2.6 not to determine the chemical structure of Submitted Compounds, or otherwise structurally modify/alter the composition of the Submitted;

4.2.7 not to use Submitted Compounds in humans;

4.2.8 not to use Submitted Compounds for any commercial use;.

4.3 For the avoidance of doubt, LEO has the right at any time; 1) to refuse receipt of the Submitted Compounds from the Institution; or 2) to decide not to conduct the Research; or 3) not to continue with the Research. In case of 2 or 3, LEO shall notify the Contact Person of such a decision and the Institution shall have the choice to either request the Submitted Compounds returned to Institution at Institution's cost or have LEO destroy the unused Submitted Compounds.

5 CONFIDENTIALITY

5.1 The only information requested by LEO regarding the Submitted Compounds is stipulated in Appendix 3. The requested information is **no**t considered by LEO as confidential information. If Institution, however, justifies that LEO will receive information in writing that Institution considers as confidential and LEO accepts the receipt of such confidential information ("Confidential Information") then any such Confidential Information shall be kept confidential by LEO. The same applies to Research Results communicated to Institution that relates to the Submitted Compounds. LEO shall not disclose Confidential Information to any third party (person or entity) or otherwise make known in any manner any part of the Research Results that relates to the Submitted Compounds without the prior written consent of Institution. If Research Results are kept confidential, Institution decides whether or not Research Result shall be made public. However Institution shall be aware that publishing Research Result may render any opportunity for a further collaboration or business relation with LEO impossible.

5.2 LEO shall only use Confidential Information and Research Results for the purpose of evaluating a possible business relationship with Institution. The confidentiality and limited use obligations shall commence on the Effective date and shall continue in force for three (3) years from the Effective Date or until Institution have published Research Results whichever comes first.

5.3 Notwithstanding the foregoing LEO may disclose Confidential Information to its duly authorized employees, employees of affiliates (defined as any company, corporation, firm, partnership or other entity controlled by LEO "Affiliate"), who need to know such Confidential Information in the course of the performance of their duties relating to this Agreement and evaluation of a potential business relationship with Institution.

5.4 The confidentiality and limited use obligation under this Agreement does not extend to Confidential Information that:

5.4.1 at the time of disclosure, is already in the public domain through no fault of LEO;

5.4.2 after disclosure, becomes a part of the public domain by disclosure, for reason other than breach of this Agreement by LEO;

5.4.3 LEO is able to prove, has been lawfully in its or any of its Affiliates' possession prior to any disclosure under this Agreement; or

5.4.4 is hereafter made available or disclosed by a third party to LEO or any of its Affiliates where such third party did not acquire such information under a still effective obligation of confidentiality to Institution.

5.4.5 Is independently developed by or for LEO or any of its Affiliates without use of, reliance on or reference to the Confidential Information, as evidenced by LEO records;

5.5 If LEO is required to disclose Confidential Information by an order or action of a governmental agency, authority or court, LEO shall inform the Institution as soon as reasonably possible by email and shall only furnish that portion of the Confidential Information which is legally required, and shall exercise all reasonable efforts required to obtain confidential treatment for such information. It is the responsibility of Institution to keep Appendix 1 updated in order for LEO to be able to contact Institution.

6 RESERVED RIGHTS

6.1 As LEO has its own research activities, there is a possibility that Institution could provide information in relation to Submitted Compounds which LEO already possesses or has access to, will develop either alone or in collaboration with third parties or may receive from third parties in the future. For this reason LEO does not wish to receive detailed information regarding the Submitted Compounds; especially no structural information, unless the structure of the Submitted Compounds already are publically available. If Institution submits Submitted Compounds with structural information, Institution hereby represents and warrants that such information is generally available to the public and accepts that LEO can disclose such irrespective of any confidentiality obligation undertaken under article 5 above. If for any reason Institution should submit any information in addition to the Submitted Compounds then LEO will return or delete such information. .

6.2 In relation to information mentioned under article 6.1 above, LEO will under no circumstances 1) accept any responsibility for such information; and 2) be bound by any kind of confidentiality or non-use obligation with respect to such information. Institution hereby accepts and confirms its understanding of this condition.

6.3 For the sake of clarity, LEO will not disclose the fact that Research took place nor publish the Research Results, unless otherwise agreed to by Institution.

7 INTELLECTUAL PROPERTY

7.1 Institution's existing intellectual property rights in Submitted Compounds shall remain with Institution unless the Parties agree otherwise in writing.

7.2 Institution accepts and agrees that the Submitted Compounds might already be known to LEO. Therefore this Agreement shall not impact the determination of inventorship of any compound known to LEO prior to or independently of submission of Submitted Compounds to LEO as evidenced by LEO records, nor shall it prevent LEO from carrying out any activities.

7.3 Institution shall be the owner of Research Results. However, Institution allows LEO to use the Research Results as stated in article 5.3 above.

8 PUBLICATION

8.1 Institution is free to publish the Research Results provided by LEO and created from Research for Submitted Compound. Institution accepts to acknowledge LEO for the work carried out in relation to Research Results and further acknowledge LEO as the source of the Research Results.

8.2 Institution undertakes to inform LEO of any type of disclosure containing the Research Results.

8.3 Institution understands that by disclosing (e.g. publishing) Research Result on Submitted Compound which LEO may be interested in testing further, Institution may jeopardize this opportunity for at future business relation or collaboration with LEO.

9 TERM

9.1 This Agreement shall come into force on the Effective Date and remain in force until terminated by either Party for any or no reason with thirty (30) days' prior written notice to the other Party or one (1) year after the Effective Date whichever comes first.

9.2 The provisions of this Agreement shall upon termination remain in force with respect to any Submitted Compounds then held by LEO. The Institution shall not ship any new Submitted Compounds to LEO. Upon termination LEO shall destroy any remaining Submitted Compounds. Institution may request confirmation by LEO in writing that such destruction has taken place. LEO may alternatively return any remaining Submitted Compounds.

10 NOTICE

10.1 Any written notice required under this Agreement shall be provided if to

Institution: See Appendix 1

LEO: **LEO Pharma A/S**, Industriparken 55, 2750 Ballerup, Denmark
Att. Niclas Nilsson, Head of R&D Open Innovation, Research
P: +45 44 94 58 88
E: niclas.nilsson@leo-pharma.com

11 MISCELLANEOUS

11.1 This Agreement constitutes the entire agreement between the Parties with respect to the subject matter hereof and supersedes all prior agreements, written or oral, between the Parties in this respect. This Agreement may not be modified, changed or discharged, fully or in part, except by an agreement in writing signed by authorised representatives of the Parties.

12 GOVERNING LAW AND VENUE

12.1 This Agreement shall be governed by the laws of Denmark without regard to the conflict of laws provisions. In the event of any dispute arising out of or relating to any provision of this Agreement, the Parties shall try to settle any such dispute amicably on a good faith basis. If the Parties are unable to solve the dispute within reasonable time, the dispute shall be settled by arbitration in Copenhagen and in accordance with the rules of arbitration procedure adopted by the Danish Institute of Arbitration ("Institute") and in force at the time when such proceedings are commenced. The arbitration tribunal shall be composed of three (3) arbitrators. Each Party shall appoint one (1) arbitrator and the Institute shall appoint one (1) arbitrator who shall be the chairman of the arbitration tribunal. If a Party has not appointed an arbitrator within thirty (30) days of having been requested hereto or received a notice of the arbitration, such arbitrator shall be appointed by the Institute. The proceedings shall be conducted in the English language.

13 SIGNATURE

13.1 This Agreement may be executed in one or more counterparts, each of which shall be deemed to be an original and all of which shall constitute together the same document. The Parties agree that signatures transmitted by electronic means (e.g. facsimile or a scanned version of the executed agreement in PDF format attached to an e-mail) shall bind the Parties.

LEO Pharma A/S	**Institution**
Date	Date
Signature	Signature
JAKOB FELDING Name (Capital letters)	Name (Capital letters)
Director, Skin Research Title	Title

APPENDIX 1 – Institution

Please provide contact information for the Institution and persons responsible for the Agreement and science, respectively.

"Institution" in this Agreement refers to:

Name of Institution:	
Address:	
Country:	
Registration Number:	
Phone and email:	
Address for receiving barcoded empty vials (if different):	
Country:	

Institution's contact person for this Agreement is ("Contact Person"):	
Name:	
Phone:	
Email:	

Institution's scientific contact person is (only if different from above):	
Name:	
Phone:	
Email:	

Contact for notices (cf. article 10.1) (only if different from above):	
Name:	
Phone:	
Email:	

APPENDIX 2 – Procedure

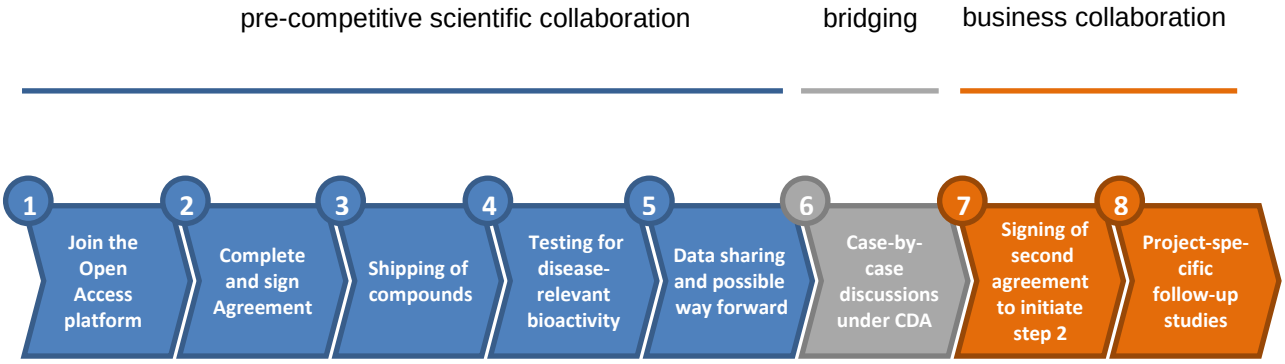


Figure. Stepwise procedure of the Open Innovation platform to test compounds for bioactivity

1. **You would like to test your compounds for effect in the disease-relevant assays**
2. **Complete and sign of the Open Innovation agreement which is mandatory and not subject to modifications**
3. **Receive barcoded vials (or plates) from LEO and return to LEO**
4. **LEO Pharma tests the compounds for bioactivity in a selection of advanced *in vitro* assays**
5. **LEO returns the Research Results within 2-3 months and, if relevant, a proposal on how to continue**
6. **If relevant: follow-up discussions based on additional information exchanged under confidentiality**
7. **Design and signing of second agreement to proceed with case-by-case specific studies**
8. **In-depth analysis of the research project aiming to find new treatment opportunities**

APPENDIX 3 – Submitted Compounds

Prior to physical shipment Institution will submit a digital nomination of the compounds, including the following information: Compound name and Molecular Weight. Upon acceptance of the compound nomination in this Appendix 3 and receiving a signed Agreement, LEO will return barcoded vials for physical shipment of the compounds.

To test up to 10 different compounds LEO require 200 ul of 10 mM DMSO solution of each compound shipped in the provided barcoded vials.

Usually normal ambient temperature during shipping is sufficient, however, if your compounds need a particular shipping requirement, please ensure so yourself. Please keep in mind, the compounds will be used in 37° C assay incubating for up to 72 hours and should therefore not be 'unstable'.

Please, fill out the compound template, one line per compound to be tested.

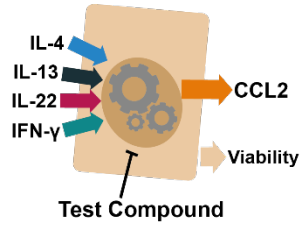
Number Compound count	**Name*** Your compound name	**MW*** mol. weight
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

* Required entries to process compound nomination for biological testing.

APPENDIX 4 – Research

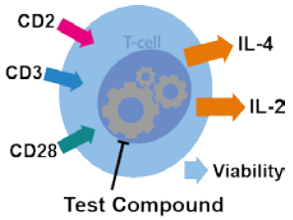
The Phenotypic and disease-relevant in vitro assays

The current assay portfolio consists of the following disease-relevant *in vitro* assays. The selection of assays used in Open Innovation projects can vary based on the compounds, scope and availability.



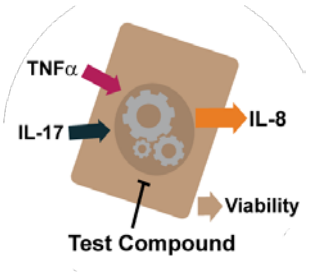
1. Eczema inflammation in human Keratinocytes

Primary human keratinocyte are stimulated using an eczema-relevant cytokine cocktail (IL-4, IL-13, IL-22 and IFN-gamma) which induce an inflammatory response measured as an increase in CCL2 secretion. Molecules are tested for ability to inhibit this inflammatory response and possible effects on cell viability.



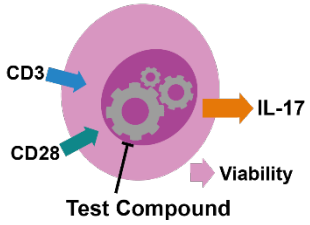
2. IL-2 and IL-4 release from primary human CD4+ T cells

Primary human purified CD4+ T cells are stimulated to produce the eczema relevant cytokines IL-2 and IL-4. Test compounds are tested for ability to inhibit this inflammatory response, as well as for any general effect on cell viability.



3. Psoriatic inflammation in human Keratinocytes

Primary human keratinocyte are stimulated using a psoriasis-relevant cytokine cocktail (TNF-alpha and IL-17) which induce an inflammatory response measured as an increase in IL-8 secretion. Test compounds are tested for ability to inhibit this inflammatory response.



4. Human PBMC release of IL-17

Human primary human PBMC (Peripheral Blood Mononuclear Cells) are isolated from blood and activated by a CD3, CD28 and IL-23 resulting in increased production of IL-17. The test compounds are tested for the ability to inhibit the IL-17 release. Secondary viability readout is also provided.

APPENDIX 5 – Example of Research Result Report

CONFIDENTIAL

The appendix illustrates an example of a Research Results report, however, the exact layout and content is subject to change due to continuous improvements.

EXAMPLE ONLY

Thank you for submitting your compounds for testing in LEO Pharma Open Innovation platform!

We have completed testing for bioactivity and the Research Results are provided in this data report.

Data Report

Reporting the Research Results obtained from testing the Submitted Compounds. Note: Although the assays are advanced functional and disease-relevant, they do not represent all possible disease-mechanisms and it is possible, even if your compound has shown efficacy in other models, that the results are negative. This simply reflects a possible limitation in the testing set-up but provides the basis for the evolution of continued collaboration.

Compounds tested:

No	Your reference	LEO reference
1	MyCMPD100	LEO12345

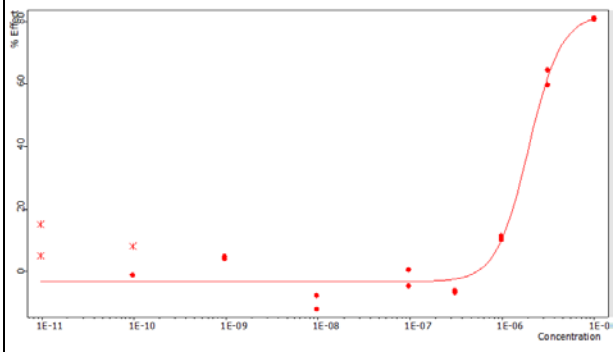
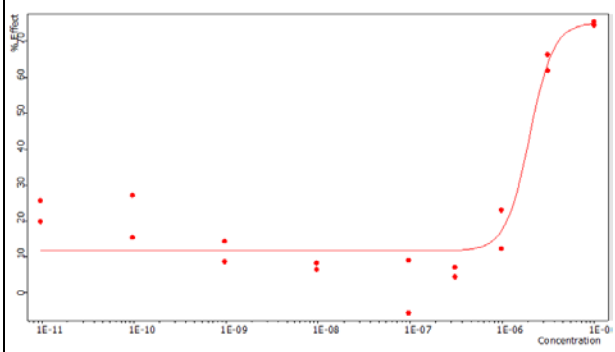
Report date: 2015-01-01

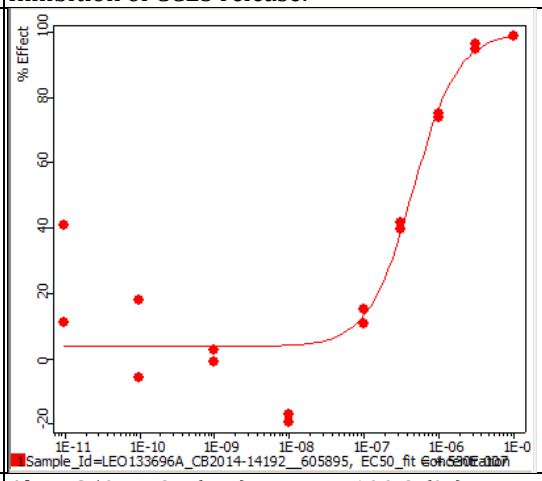
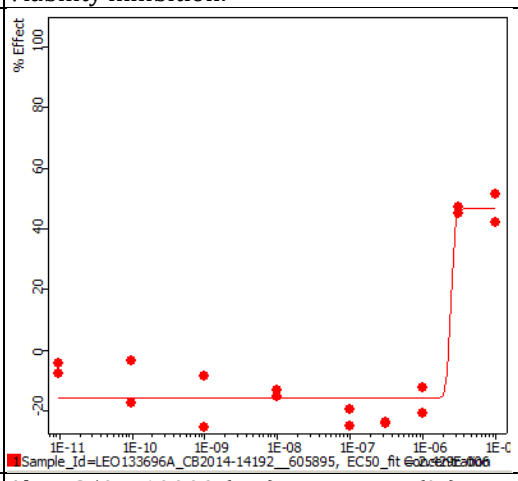
Based on these Research Results LEO has no immediate intention to pursue the specific compound.

Comment:

The compounds show a general 'anti-inflammatory' effect. However due to, an often matched, drop in cell viability the anti-inflammatory effect can't be distinguished from a cytotoxic effect. Probably the most interesting result is observed in the eczema assay. Here the effect on viability is much lesser - indicating the compound has pharmacological relevant effect on the CCL5 producing/releasing pathway. The potency is low-medium and the EC50 would preferably be lower in order to be of immediate interest.

EXAMPLE ONLY

Cmpd no	Your reference:	LEO Pharma reference:
1	MyCMPD100	LEO12345
Assay:	Psoriasis-like induced IL-8 release from human primary Keratinocytes	
	Inhibition of IL-8 release:	Viability inhibition:
		
	Abs EC50 = 2370 (nM), Emax = 84.4 (%)	Abs EC50 = 2240 (nM), Emax = 75.4 (%)
	Comment: Very low potency effect on inhibiting IL-8 release is matched by similar drop in viability.	

Cmpd no	Your reference:	LEO Pharma reference:
1	MyCMPD100	LEO12345
Assay:	Eczema-relevant induced CCL5 release from human primary Keratinocytes	
	Inhibition of CCL5 release:	Viability inhibition:
		
	Abs EC50 = 427 (nM), Emax = 100.2 (%)	Abs EC50 = 10000 (nM), Emax = 47 (%)
	Comment: Low-medium potency effect on inhibiting CCLR5, only partial effect on viability, possibly cytostatic.	