



HOSPITAL GRANT AGREEMENT

This Grant Agreement ("**Agreement**") is entered into as of [01/03/2016] ("**Effective Date**") by and between Novartis Healthcare A/S, Reg. No. 20575786, a company incorporated under the laws of Denmark, located at Edvard Thomsens Vej 14, DK-2300 Copenhagen S, Denmark ("**Novartis**") and [Bent Winding Deleuran, Consultant, DMSc, Department of Rheumatology Aarhus University Hospital and Department of Biomedicine, Aarhus University, a not-for-profit research and educational institution incorporated under the laws of Denmark, located at Wilhelm Meyers Alle 4, 8000 Aarhus C, Denmark ("**Institution**")], ("**Grant Recipient**"). Novartis and Grant Recipient may hereinafter be referred to individually as a "**Party**" and collectively as the "**Parties**".

WHEREAS, Grant Recipient has specifically requested Novartis' financial contribution in order to support the Grant Activity (as defined in Exhibit A), through a Grant Request Letter, which is attached hereto as Exhibit B;

WHEREAS, in accordance with the Grant Request Letter mentioned above, Novartis wishes to support the Grant Activity with the grant amount or grant in-kind ("**Grant**") (as defined in Exhibit A); and

WHEREAS, Grant Recipient accepts the Grant subject to the terms and conditions of this Agreement.

NOW THEREFORE, in consideration of the premises and the mutual covenants herein contained, it is mutually agreed as follows:

1. GRANT BY NOVARTIS

- 1.1 **Grant.** Novartis will provide the Grant as set forth in Exhibit A solely to support Grant Recipient in performing the Grant Activity as set forth in Exhibit A in accordance with agreed timelines if any..
- 1.2 **Statement of Purpose.** The Grant Activity is for scientific and/or educational purposes only and will not promote Novartis' products, directly or indirectly. The Grant is not being given in exchange for any explicit or implicit agreement to purchase, prescribe, recommend, influence or provide favorable formulary status for any of Novartis' products. The Grant is based upon a budget provided to Novartis by Grant Recipient reflecting a good faith estimate of the actual cost of the Grant Activity. The Grant has not been determined in a manner that takes into account the volume or value of referrals or business, if any, generated between Novartis and Grant Recipient or any of their respective officers, directors, employees, agents, affiliates, parents or subsidiaries.
- 1.3 **Novartis Responsibility.** Grant Recipient agrees that Novartis' responsibility is solely to provide the Grant. Novartis will not be liable to Grant Recipient or to any other person for the Grant Activity or the use of the Grant (including any claims or losses related thereto). Novartis may terminate this Agreement and require Grant Recipient to return the Grant and take other corrective action if Grant Recipient breaches this Agreement.



2. OBLIGATIONS OF GRANT RECIPIENT

2.1 Use of Grant.

- (a) Grant Recipient verifies by signing this Agreement that the Grant Recipient is willing to receive the Grant.
- (b) Grant Recipient has appointed Activity and Amount Manager(s) to manage the Grant and the Grant Activities as set forth in Exhibit A.
- (c) Grant Recipient shall use the Grant solely for the Grant Activity and shall not use the Grant for any activity that is inconsistent with, or prohibited by any law, rule or regulation. The Grant Recipient undertakes to independently contact Novartis in the event any part of the Grant has not been used for the Grant Activity so that such amount can be refunded to Novartis without undue delay.
- (d) Grant Recipient will comply with (and shall be solely responsible for any failure to comply with) all relevant laws, rules and regulations (including any code of practice or other guidelines generally followed by pharmaceutical companies in the relevant country) in connection with the Grant Activity. Grant Recipient warrants that the Grant Activity is compliant with all such requirements.
- (e) Grant Recipient is solely responsible for the manner in which the Grant is disbursed, recorded and accounted and for all contractual and other relationships with third parties relating to the Grant Activity and the use of the Grant. Any claims for payment from third parties involved in the Grant Activity are the sole responsibility of Grant Recipient and Novartis will not fund any additional amounts for the Grant Activity.

2.2 Objectivity & Balance.

The Grant Activity will be independent, non-promotional and free from commercial influence or bias.

- (a) If the Grant Activity involves the discussion of Novartis products, or the comparison of Novartis products with other products, that discussion and/or comparison must be objective, balanced, accurate, not misleading or deceptive and in compliance with all applicable laws, rules and regulations. Where appropriate, the Grant Activity will include a discussion of multiple treatment options, and will not focus on a single product.
- (b) Grant Recipient will ensure that any titles or overview information relating to the Grant Activity will fairly and accurately represent the scope of the planned activity.



- (c) If required, Grant Recipient is responsible for selection of presenters, moderators and collaborators for the Grant Activity. Novartis will not control the planning, content, speaker selection or execution of any Grant Activity. If Novartis suggests presenters, moderators or collaborators, Grant Recipient will record the role of Novartis in making the suggestion, seek other sources and make a final selection based on balance and independence.

2.3 Disclosure of Financial Relationships.

- (a) Grant Recipient will: (i) disclose, to all audiences and in all publications relating to the Grant Activity, that Novartis has provided a grant to support the Grant Activity; (ii) acknowledge support from Novartis in brochures, syllabi, and other materials related to the Grant Activity; and (iii) disclose any other relationships Novartis has with any individual speakers, moderators, collaborators or Grant Recipient which a reasonable and ethical person would expect to be disclosed.
- (b) Novartis may disclose publicly the financial and non-financial support provided to Grant Recipient, including, without limitation, the Grant Recipient's identity, the Grant and purpose of the support.

2.4 Ancillary Activities.

- (a) If the Grant Activity occurs as part of an overall activity that includes commercial activities, such activities will neither influence planning nor interfere with the Grant Activity. No commercial activities will be permitted in the same room as an educational activity, unless (i) this is allowed in the country in which the activity will take place and (ii) only to the extent that such commercial activity does not interfere with the purpose of the Grant Activity.
- (b) The scheduling of meals and/or receptions, if any, in connection with any portion of the Grant Activity is at the sole discretion of Grant Recipient. Meals and/or receptions, if any, will be modest and conducive to the Grant Activity, and the amount of time at the meals or receptions will be clearly subordinate to the overall amount of time.
- (c) Reconciliation of Expenses. At the conclusion of the Grant Activity, Grant Recipient will provide to Novartis a reconciliation of the actual expenses versus estimated expenses and will issue a refund to Novartis for any portion of the Grant not incurred in the implementation of the Grant Activity. In addition, Grant Recipient will retain appropriate records of the Grant Activity and the use of the Grant and will provide copies of the records to Novartis on request to confirm that the Grant has been used in accordance with this Agreement.

3. GENERAL

- 3.1 **Entire Agreement.** This Agreement, together with its Exhibits, sets forth the entire agreement and understanding of the Parties as to the subject matter hereof and supersedes all proposals, oral or written, and all other prior communications between the Parties with respect to such subject matter. In the event of any conflict between a substantive provision of this Agreement and any Exhibit hereto, the substantive provisions of this Agreement shall prevail.



- 3.2 **Governing Law and Jurisdiction.** This Agreement shall be governed by and construed under the laws of Denmark, without giving effect to the conflicts of laws provision thereof. Any dispute or claim arising out of or in connection with this Agreement which cannot be settled amicably between the Parties, is to be brought before the Maritime and Commercial Court in Copenhagen or, if this court is not competent, before a competent court of law in the Kingdom of Denmark.
- 3.3 **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the Parties intending to be bound have caused this Agreement to be executed by their duly authorized representatives.

NOVARTIS HEALTHCARE A/S

Novartis signature 1-contract owner

By: Monika Mortensen

Name: **Monika Mortensen**

Title: **MSc, PhD, MSL**

Date: **29/02/2016**

Novartis signature 2-Business Approver

By: Peter Drøidal

Name: **Peter Drøidal**

Title: **Nordic Head Immunology & Dermatology,
Country Manager, Denmark**

Date: **05.04.16**

Bent Winding Deleuran,

Professor, consultant, DMSc, Department of Immunology, Institute of Biomedicine, Aarhus University, Bartholins Alle 4, Building 1242, DK-8000 Aarhus C, Denmark

By: Bent Winding Deleuran

Name: **Bent Winding Deleuran**

Title: **Consultant, DMSc**

Date: **24/03/2016**



EXHIBIT A

GRANT & GRANT ACTIVITY

Grant amount: [120.000,00] DKK and/or

Grant in-kind: [Research Grant]

Grant Activity: Title: **Interactions between IL-26 and IL-17A in Spondyloarthritis**

Background: Spondyloarthritis (SpA) is a chronic inflammatory disease involving joints and especially the ligaments of the spine. The disease is characterized by mineralization of the spinal ligaments, resulting in fusion of the spine and sacroiliac (SI) joints. The disease can also involve body surfaces e.g. skin, gut and urine tract. The CD4 T-cell sub-profile, called TH17, is named after its most well known member IL-17A and is believed to be heavily involved in SpA. This is confirmed by recent treatment with anti-IL-17A antibodies showing profound efficacy in diseases associated with SpA. Differentiation into TH17 cells is quite complicated, but sustained growth of TH17 cells has in vitro been possible by the addition of IL-23. It has also been shown that mice, which lack the IL-23R, have very low numbers of TH17 cells. We have recently shown that progression of disease in SpA is not likely to involve the IL-23R-pathway (For detail, please see Thomas Andersen's PhD, unpublished). Antibody treatments towards many other cytokines connected with the development of TH17 cells have shown little promise in SpA. This suggests that there could be other candidates that could play an important role in regulating the growth of TH17 cells in SpA. Recently, IL-26 has come into focus. IL-26 is produced in high amounts by Fibroblast likesynovial cells (FLS), and can sustain TH17-growth. The reason that this cytokine has been given so little interest is that it is not found in mice. IL-26 is thus produced by the cells often found in the ligaments and can sustain growth of TH17-cells.

Aim

We want to investigate if IL-26 could be the dominant growth factor for TH17 cells in SpA.

Methods

We are using samples from biobanks, cell cultures, cell separation based on cytokine secretion, ELISA, PCR, immunohistochemistry, immunofluorescence, CHIP-assay, bioassay for receptors, Western blotting, ex vivo cultures from inflamed joints, and animal models.

Ethics

The Local Ethical Committee and the Danish Data Protection Agency have approved all the projects.

Research environment

The research group for inflammatory rheumatic diseases in Aarhus is established as collaboration between Department of Rheumatology, Aarhus University Hospital and Institute for Biomedicine, Aarhus University. The work is based in the field of translational medicine, combining clinical studies at the hospital with basal studies at the university. This is done to improve our understanding of arthritis, hopefully resulting in better treatments for patients.

Staff:

- Bent Deleuran, Professor, consultant, DMSc, Department of Rheumatology, Aarhus University Hospital and Department of Medical Microbiology and Immunology, Aarhus University (Head of project, short CV included)
- Malene Hvid, cand.scient, PhD, associate professor
- Tue Kragstrup, MD, PhD



Perspectives: Clarifying the pathogenic mechanisms that enable growth of IL-17A positive T-cells. This will give a better understanding of the processes in SpA and possible also create new biomarkers for SpA that could be useful in identifying SpA patients that are anti-IL-17A candidates. With our large biobanks and other facilities we have the possibility to study this in great detail.

Finance: We are applying Novartis for the sum of 120,000 DDK. This accounts for materials in the daily running of the laboratory, e.g., antibodies, PCR reagents, plastic, buffers, flow, cell cultures, etc. (For details please see included budget) The Danish Rheumatoid Association has supported the program with 75,000 DDK and NOVO has supported it with 120,000 DKK for at research year student.



The Grant Amount shall be paid by Novartis to the following bank and bank account:

Bank: Danske Bank

Adresse: Girostrøget 1, 0800 Høje Taastrup

Reg./bankkonto: 0216 – 4069053238

Vort CVR. Nr.: 31119103

Tekst ved overf.: Bent Deleuran

When effectuating the payment Novartis will include the following reference:

The following Activity Manager shall manage the Grant Activity:

Bent Deleuran,

Professor, consultant, DMSc.

Department of Immunology, Institute of Biomedicine, Aarhus University, Bartholins Alle 4, Building 1242, DK-8000 Aarhus C, Denmark

Direct Tel number: +45 87167839

Bent Winding Deleuran <bd@biomed.au.dk>

The following Amount Manager shall manage any Grant Amount provided under this Agreement and ensure that the Grant Amount is transferred to the correct hospital account. This Amount Manager will also ensure that any grant in-kind is delivered to the correct hospital division:

Merete Kamp,

Project economist

HE Administrative Centre - HE Finance, Katrinebjergvej 89 F, building 5132, 8200 Aarhus N, Denmark

merete.kamp@au.dk

Mobile: 51447585