HOSPITAL GRANT AGREEMENT

This Grant Agreement ("**Agreement**") is entered into as of 26.04.2017 ("**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 Rigshospitalet-Glostrup, HovedOrtoCenteret – Øjenklinikken, incorporated under the laws of Denmark, located at Nordre Ringvej 57, 2600 Glostrup, ("**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

Rasmus Olsen

By: _____

Name: Rasmus Olsen

Title: Medical Science Liaison

Date: 19/5-17

Maja Hugod

By: _____

Name: MAJA HUGOD

Title: Nordic Medical Franchise Head

Date: 19/5 - 17

Rigshospitalet - Glostrup

By: _____

Name: ~~Daniella Bach Helm~~

Title: Uddannelsesansvarlig overlæge
~~Klinisk Lektor - PhD FEBO~~
Øjenklinikken
~~Rigshospitalet - Glostrup~~

Date: JUNE 15, 2017

EXHIBIT A

GRANT & GRANT ACTIVITY

Grant amount: 15 months lease of Triton OCT-1 DRI plus sn. 207057, inkl. Triton OCT-1 PC, sn. 6Q001029TN, with ImageNet 6 software sn. 519500009 / C6BC18DB, monitor and keyboard. ATE-800 Instrument table w. PC holder. (**Total leasing value: 285.000 DKK**)

Grant Activity: See Enclosed grant request in Exhibit B. The request is supported by a research grant covering the lease of the Triton OCT-1 DRI plus machine (as specified aboved) in the research period from 1st of May 2017 to 1st of August 2018.

The grant amount is paid by Novartis directly to the Machine vendor (Topcon Danmark, CVR: 26505259) on behalf on the grant recipient. No direct payment to the grant recipient.

The following Activity Manager shall manage the Grant Activity:

Daniella Bach-Holm, PhD, FEBO
Klinisk lektor, Uddannelsesansvarlig overlæge, Leder af glaukomteamet
Rigshospitalet – Glostrup
HovedOrtoCentret - Øjenklinikken
Ndr Ringvej 57
2600 Glostrup
Direct Phone: +45 38 63 40 04
E-mail: daniella.bach-holm.01@regionh.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:

Daniella Bach-Holm, PhD, FEBO
Klinisk lektor, Uddannelsesansvarlig overlæge, Leder af glaukomteamet
Rigshospitalet – Glostrup
HovedOrtoCentret - Øjenklinikken
Ndr Ringvej 57
2600 Glostrup
Direct Phone: +45 38 63 40 04
E-mail: daniella.bach-holm.01@regionh.dk

EXHIBIT B

GRANT REQUEST LETTER INCLUDING BUDGET

Kontrastfri angiografi af synsnerve og nethinde mhp undersøgelse af, hvorledes karrene reagerer, når patienter med grøn stær får foretaget en tryk-sænkende operation

Line Kessel, overlæge, PhD

Daniella Bach-Holm, overlæge, PhD

Øjenklinikken, Rigshospitalet – Glostrup og Københavns Universitet

Glaukom (grøn stær) er en langsomt progredierende synsnervelidelse, der ubehandlet ødelægger synsnerven medførende, at patienterne får påvirket perifert synsfelt, så der er nogle områder i deres synsfelt, hvor de ser dårligt. Langt hen i sygdomsforløbet bliver patienterne ved med at beholde deres centralsyn - men sygdommen kan progrediere yderligere og forårsage blindhed.

Den vigtigste behandlelige risiko-faktor for grøn stær er øjentrykket. Hvis trykket i øjet er for højt i forhold til hvad nethinde og synsnerve kan holde til, ødelægges gangliecellelaget i nethinden samt nervefibrene i synsnervehovedet (papillen) og nethinden. Man mener, at en af årsagerne til, at dette sker, er, at det høje øjentryk påvirker blodforsyningen til disse strukturer givende iltmangel (iskæmi). Derfor mener man også, at hvis man på forskellige måder kan øge blodforsyningen, kan man mindske skaderne ved glaukom

Blodgennemstrømningen i nethinden og synsnerven har altid været vanskeligt at måle ikke-invasivt og reproducerbart.

Optisk kohærenstomografisk angiografi (OCTA) er en nyere ikke-invasiv metode til undersøgelse af karsygdom i nethinden. Teknikken har primært været brugt til diagnostik af retinale neovaskularisationer (nye kar i nethinden) ved AMD (aldersrelateret macula-degeneration – forkalkninger på nethinden), men der er også mulighed for at se og måle blodgennemstrømningen i synsnerven (se nedenstående foto)[1]. Det er vist at der er færre kapillærer omkring synsnerverne på patienter med åbenvinklet glaukom og at der bliver færre, jo mere udtalte synsfeltsdefekterne er.[1]

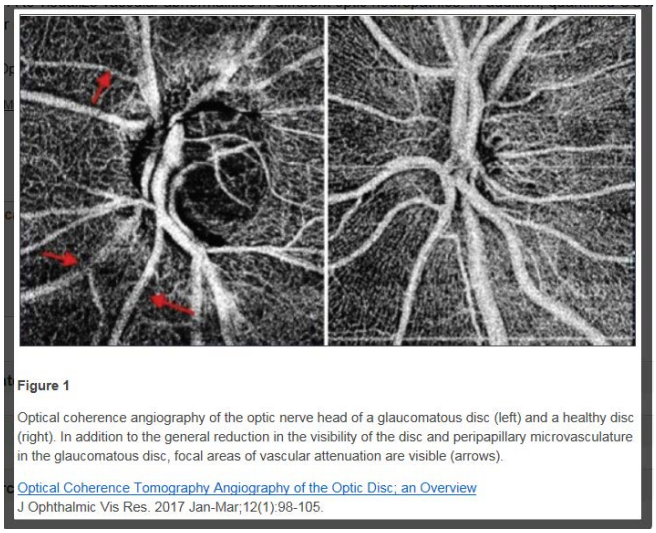

Figure 1

Optical coherence angiography of the optic nerve head of a glaucomatous disc (left) and a healthy disc (right). In addition to the general reduction in the visibility of the disc and peripapillary microvasculature in the glaucomatous disc, focal areas of vascular attenuation are visible (arrows).

Optical Coherence Tomography Angiography of the Optic Disc: an Overview
J Ophthalmic Vis Res. 2017 Jan-Mar;12(1):98-105.

Der er ikke beskrevet meget omkring glaukomsygdommen og den peripapillære og retinale kartæthed og brugen af angio-OCT. Det kunne være særdeles interessant at blive mere fortrolig i brugen af denne teknik hos glaukom-patienter – mhp at beskrive hvilke retinale og papillære kar-forandringer der er karakteristiske for sygdommen – både i (differential)diagnostisk øjenmed men også mhp at vurdere effekten af forskellige typer behandlinger.

Vi ønsker bl.a. at beskrive, hvordan acetazolamid påvirker den peripapillære og retinale blodgennemstrømning – både hos raske og hos patienter med glaukom. Herudover ønsker vi også at beskrive effekten af kirurgisk tryk-sænkende procedurer på blodgennemstrømningen.

Derfor ansøger vi hermed Novartis om finansiering af leasingen af Swept Source OCT angio fra til Øjenklinikken, Rigshospitalet – Glostrup, således at vi nøjere kan forske sammenhængen mellem glaukom og den peripapillære og retinale blodgennemstrømning samt undersøge effekten af forskellige indgreb på dette.

Vi påregner, at projektet kører fra 1. april 2017 til 1. august 2018.

[1]Wang X, Jiang C, Ko T, Kong X, Yu X, Min W, Shi G, Sun X: *Correlation between optic disc perfusion and glaucomatous severity in patients with open-angle glaucoma: an optical coherence tomography angiography study.* Graefes Arch Clin Exp Ophthalmol. 2015 Sep;253(9):1557-64.