GRANT AGREEMENT

This Grant Agreement ("**Agreement**") is entered into as of 4th of December 2018 ("**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 Klinik for Klinisk Fysiologi, Nuclear Medicin & PET, Rigshospitalet, a hospital department incorporated under the laws of Denmark, located at Blegdamsvej 9, 2100 København Ø, ("**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 (as defined in Exhibit A); and

WHEREAS, Grant Recipient accepts the Grant Amount 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 Amount as set forth in Exhibit A solely to support Grant Recipient in performing the Grant Activity as set forth in Exhibit A.

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 Amount 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 Amount 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 Amount 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 Amount. Novartis will not be liable to Grant Recipient or to any other person for the Grant Activity or the use of the Grant Amount (including any claims or losses related thereto). Novartis may terminate this Agreement and require Grant Recipient to return the Grant Amount and take other corrective action if Grant Recipient breaches this Agreement.

2. OBLIGATIONS OF GRANT RECIPIENT

2.1 **Use of Grant Amount**.

(a) Grant Recipient shall use the Grant Amount solely for the Grant Activity and shall not use the Grant Amount 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 Amount has not been used for the Grant Activity so that such amount can be refunded to Novartis without undue delay.

(b) 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.

(c) Grant Recipient is solely responsible for the manner in which the Grant Amount 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 Amount. 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**.

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

(b) 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.

(c) 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.

(d) 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 Amount 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 Amount 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 Amount and will provide evidences (as further specified in Exhibit A) to Novartis to document that the Grant Amount 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

Date: 04-Dec-2018 | 5:33:44 AM EST

Signature: DocuSigned by: Elisabet Oladottir 6460C1B340804AD...

By: Elisabet Oladottir

Title: Medical Advisor

Signature: DocuSigned by: Erik Heegaard 65E1D5659F45487...

By: Erik Heegaard

Title: Medical Director Nordics

Klinik for Fysiologi, Nuclear Medicin & PET

Date: 10-Dec-2018 | 7:11:47 AM EST

Signature: DocuSigned by: Andreas Kjaer F252E0075EFD48E...

By: Andreas Kjær

Title: Professor, ph.d, dr.med

EXHIBIT A

GRANT AMOUNT & GRANT ACTIVITY

Grant Amount: ***200.000*** DKK

Grant Activity: Funding of a scientific research project “Angiogenese PET/CT of patients with neuroendocrine neoplasmas”. The aim of the project is to investigate the use of angiogenese PET/CT with the tracer ^{68}Ga-NODAGA-E[c(RGDyK)]$_2$ for a prognostik evaluation of patients with neuroendocrine neoplasmas (NEN).

The grant can be used to fund materials (PET tracer and tissue analysis).

Evidences must be provided to Novartis upon completion of the Grant Activity:

The grant recipient is required to confirm to Novartis within two months from conducting the activity that the grant has been used for the purpose intended by submitting the final budget of the project.

The Grant amount is payable against the corresponding invoice within sixty (60) days of its receipt and at the end of a calendar month.

The invoice shall include all details (including a Purchase Order Number) as specified in the Purchase Order received by Grant Recipient at the following email address: akjaer@sund.ku.dk

EXHIBIT B

GRANT REQUEST LETTER

Elisabet Oladottir
Medical Advisor, Oncology
Novartis Healthcare A/S
Edvard Thomsens Vej 14, 3. sal
DK-2300 Copenhagen S
DENMARK

15. november 2018

Hermed ansøges Novartis Healthcare A/S om forskningsstøtte på 200.000 kr. for året 2018 til projektet *Angiogenese PET/CT af patienter med neuroendokrine tumorer.*

Projektet undersøger anvendelsen af en ny PET tracer i neuroendokrine tumorer. Såfremt disse resultater er lovende, forventer vi at denne form for PET skanning kan benyttes til at udvælge og følge patienter i anti-angiogenesebehandling og dermed understøtte praktisering af *præcisionsmedicin.*

Der vedhæftes

- Projektbeskrivelse inkl. budget

Vi håber meget, at Novartis har mulighed for at støtte projektet.

Med venlig hilsen

Andreas Kjær
Professor, phd, dr. med.
Klinik for Klinisk Fysiologi, Nuclear Medicin & PET
Neuroendocrine Tumor Centre of Excellence
Rigshospitalet
Københavns Universitet

Angiogenese PET/CT af patienter med neuroendokrine neoplasmer.

Formål: At undersøge anvendeligheden af angiogenese PET/CT med sporstoffet ^{68}Ga-NODAGA-E[c(RGDyK)]$_2$ til prognostisk vurdering af patienter med neuroendokrine neoplasmer (NEN)..

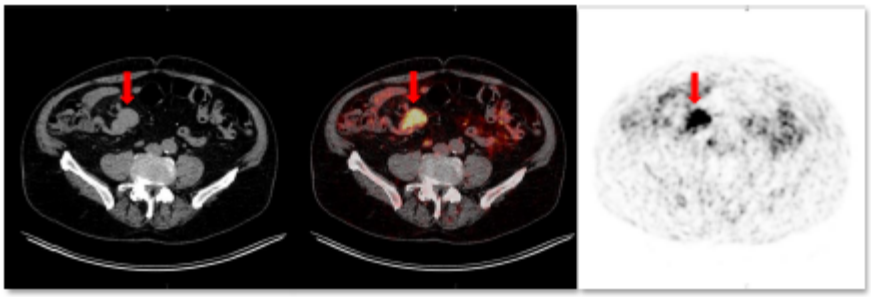
Baggrund: NEN er en sjælden form for kræft, der oftest udvikler sig i mave-tarm-kanalen (ca. 70 %) eller lungerne (ca. 25 %). NEN inddeles i tre sværhedsgrader (Grad 1-3) på baggrund af cellernes differentiering og delingsaktivitet. På baggrund af graderingen og andre faktorer tilbydes patienterne forskellige behandlingsregimer, men der mangler fortsat metoder til at bestemme hvilke patienter, der vil drage fordel af en mere intensiv behandling.

Perspektiv: Det er karakteristisk for neuroendokrine neoplasmer (kræft), at der er særlig mange blodkar i kræftvævet og graden af karnydannelse i kræftvævet har prognostisk betydning. Angiogenese-hæmmere er en nyere behandlingsform, der virker mod nydannelse af blodkar i kræftvævet. Endvidere virker mTOR inhibitorer som Everolimus også delvist gennem angiogenesehæmning. Imidlertid er det ikke alle, der vil få gavn af disse behandlinger, og det vil derfor være en fordel at kunne identificere de patienter, hvis kræftvæv danner særligt mange nye kar. Sporstoffet ^{68}Ga-NODAGA-E[c(RGDyK)]$_2$, der er udviklet af os og kun tilgængeligt på Rigshospitalet (Figur 1), visualiserer Arg-Gly-Asp (RGD) sekvenser, der binder til $\alpha v\beta 3$ integrin, som udtrykkes på overfladen af nydannede blodkar. Således vil angiogenese-PET/CT forhåbentlig kunne anvendes til prognosticering af patienter samt udvælgelse af patienter til behandling med angiogenese-hæmmere og mTOR inhibitorer efter princippet "tailored therapy".

Design: 120 konsekutive patienter med neuroendokrine neoplasmer inkluderes fra Endokrinologisk afdeling og Onkologisk afdeling, Rigshospitalet. Efter angiogenese-PET skanningen følges patienterne i 12 måneder med hensyn til progression af sygdommen/overlevelse. For de patienter, der gennemgår planlagt operation eller tumorbiopsier efter angiogenese-PET (<2 uger), vil optagelsen af ^{68}Ga-NODAGA-E[c(RGDyK)]$_2$ blive sammenlignet med genekspression af angiogenese markører.

Studiet er GCP-monitoreret og godkendt ved Lægemiddelstyrelsen, Videnskabsetisk Komite og Datatilsynet.

Status: 31 patienter er blevet skannet siden december 2017. Yderligere 6 patienter er inkluderet og afventer skanning.



Figur 1: Angiogenese PET/CT i patient med NET udgående fra mave-tarm-kanalen. Der ses kraftigt optag af sporstoffet ^{68}Ga-NODAGA-E[c(RGDyK)]$_2$ som udtryk for nydannelse af blodkar i tumoren.

Budget

	2018	2019	2020
Patients scanned	35	45	40
Materials (PET tracer)*	210.000	270.000	240.000
Materials (Tissue analysis) §	40.000	50.000	40.000
Personnel (radiochemistry) #	35.000	45.000	40.000
Technologists #	35.000	45.000	40.000
Image evaluation (PET + Radiology) #	17.500	22.500	20.000
Total	337.500	432.500	380.000

Applied for from Novartis for 2018: 200.000

* PET tracer production (cost price)

§ IHC, PCR and NGS. Granted or applied for from private foundations (Kræftens Bekæmpelse etc)

Co-financing by department