PATENT ASSIGNMENT COVER SHEET

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Stylesheet Version v1.2

EPAS ID: PAT6666063

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

CONVEYING PARTY DATA

Name	Execution Date
ITI SCOTLAND LIMITED	11/25/2020

RECEIVING PARTY DATA

Name:	SYNPEPTICA LIMITED
Street Address:	TAY-MAR, FLOCKLONES
Internal Address:	INVERGOWRIE
City:	DUNDEE
State/Country:	SCOTLAND
Postal Code:	DD2 5LE

PROPERTY NUMBERS Total: 1

Property Type	Number
Patent Number:	7892772

CORRESPONDENCE DATA

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Correspondent Name: OBLON, ET AL.
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ATTORNEY DOCKET NUMBER:	303988US
NAME OF SUBMITTER:	ELLEN MURABITO
SIGNATURE:	/ELLEN MURABITO/
DATE SIGNED:	04/20/2021

Total Attachments: 7
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Agreed Short Form Assignation

ASSIGNATION

by

(1) **ITI SCOTLAND LIMITED**, a company incorporated in Scotland with registered number SC251900 and having its registered office at Fourth Floor, Atrium Court, 50 Waterloo Street, Glasgow, G2 6HQ (the "**Assignor**"); and

in favour of

(2) SynPeptica **LIMITED**, a company incorporated in Scotland with registered number SC681137 and having its registered office at Tay-Mar, Flocklones, Invergowrie, Dundee, DD2 5LE (the "**Assignee**")

WHEREAS

(A) The Assignor wishes to transfer ownership of the Assigned IP (as defined below) to the Assignee and the parties wish to record the terms of such assignation in writing.

NOW THE PARTIES AGREE AS FOLLOWS:

1. Definitions and Interpretation

1.1 In this Assignation, the following terms and expressions shall have the meanings set opposite them:

"Assigned IP"	means any and all Intellectual Property Rights, Know How and Materials either owned by ITI under the Research and Development Agreements and any sub-contracts thereto, as set out in Parts 1-4 of the Schedule relating to the ITI Ubiquitin Proteasome System research programme, or purchased or otherwise acquired by ITI in connection with this research programme as set out in Part 5 of the Schedule. other than the Retained Materials. For the avoidance of doubt, this shall include, but not be limited to, the Intellectual Property Rights, Know How and Materials referred to in Part 6 of the Schedule together with all patents which may be granted pursuant to such patent applications; (ii) patent applications and patents which may be made or granted and claiming priority from the said patent application; and (iii) all reissues, divisions, continuations, renewals and extensions of all such patent applications and patents including supplementary protection certificates;
"Effective Date"	means the last date of signing of this Assignation;
"Know How"	means all ideas, concepts, inventions, experience, drawings, documents, designs, models, computer programs and codes, texts, records, operating and testing procedures, instruction manuals, software, algorithms, bills of materials, tables of operating conditions, specifications, data, formulae, processes and process techniques and any other technical or confidential information in any form or medium relating to the technology generated under the Research and Development Agreements and any sub-contracts theretoin Parts 1-4 of the Schedule;
"Intellectual Property Rights"	means any and all intellectual property rights or industrial rights of any description anywhere in the world including without limitation to the foregoing generality any patent applications, patents, trade marks, domain names, registered designs, copyright (including without limitation to the foregoing generality rights in computer software, object and source code), rights in the nature of copyright, biological or other materials,

	database rights, semi-conductor topography rights, unregistered design rights, rights in and to trade names, business names, product names and logos, trade secrets, know-how and any analogous or similar right in any jurisdiction (whether any such rights referred to in this definition are registered, unregistered, registerable or not and any applications or rights to apply for registration of any of them together with any registered rights resulting from any such applications or rights to apply for registration);
"Materials"	any and all physical materials relating to or embodying any of the Assigned IP and/or Technical Information including but not limited to chemical compounds, DNA constructs and cell lines, technical documentation, drawings, models, papers, plans, reports, preparatory design materials and prototypes (in each case in whatever medium they may be stored); "Retained Materials" shall mean the Materials listed in Part 7 of the Schedule.
"Schedule"	means the Schedule in Six Parts annexed to and forming part of this Assignation; and
"Technical Information"	all ideas, designs, calculations, drawings, software or codes, experience, specifications, models, formulae, processes, data, composites of materials, research, procedures and other technical information relating to the Assigned IP and/or its creation development and/or use.

1.2 The Assignation shall be interpreted in accordance with the following provisions:

1.2.1 headings are for convenience only and shall not affect interpretation and references to clauses and the schedule are to the clauses of and schedule to this Assignation; and

1.2.2 unless the context requires otherwise, the singular shall include the plural and vice versa; reference to one gender shall include all other genders; and references to persons shall include an individual, company, partnership or any other association or organisation (whether or not having a separate legal personality)

2. Assignation

2.1 In consideration of the sum of [redacted] paid by the Assignee to the Assignor (receipt of which the Assignor acknowledges receipt), the Assignor hereby confirms the assignation, transfer, conveyance and delivery to the Assignee all right, title and interest past, present and future in and to all such Assigned IP with effect from the Effective Date and any rights of any nature which may accrue to the Assignor in respect of the Assigned IP together with:

2.1.1 any and all goodwill attached thereto;

2.1.2 all the rights, powers, privileges and immunities and advantages conferred on the proprietor thereof;

2.1.3 all causes or rights of action, actual or contingent and the right to recover damages therefore in respect of any past, existing or future infringements of the Assigned IP; and

2.1.4 any and all common law rights and remedies in relation to the Assigned IP available to the Assignor as at the Effective Date.

3. General

3.1 Variation

None of the provisions of this Assignation may be varied, waived, extended or modified except expressly in writing and signed by each of the parties.

3.2 Applicable law and jurisdiction

This Assignation (including any contractual and non-contractual claims) shall be governed by and interpreted in accordance with Scots law. The parties submit to the exclusive jurisdiction of the Scottish courts.

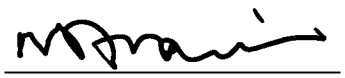
IN WITNESS WHEREOF these presents consisting of this and the two preceding pages and the schedule are executed as follows:

For and on behalf of **ITI Scotland Limited**

By *Neil Francis*

A Director thereof at *Glasgow*

On the *25th day of November 2020*



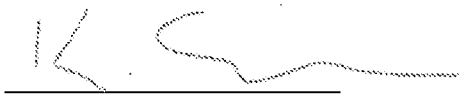
Director

For and on behalf of **SynPeptica Limited**

By *Dr Karen Sullivan*

A Director thereof at Flocklones, Invergowrie

On the 25th day of November 2020



Director

This is the Schedule referred to in the foregoing Assignation between ITI Scotland Limited and SynPeptica Limited

SCHEDULE

Part 1 Executed RDA University of Edinburgh

The Research & Development Agreement signed between ITI Scotland Ltd and the University of Edinburgh dated 29th August 2008 and the 1st September 2008 for the value of [redacted] Work Packages 1, 2A and 3, to develop assay & reagent technologies to identify novel druggable targets; clinically validate targets; and develop assay and reagents to identify peptides and small molecule modulators for drug discovery in ubiquitin area.

Part 2 Executed RDA University of Glasgow

The Research & Development Agreement signed between ITI Scotland Ltd and the University of Glasgow dated the 10th and 14th November 2008 for the value of [redacted] Work package 2 of the Ubiquitin Proteasome research programme to validate target sites using peptide array technologies.

Part 3 Executed RDA University of Strathclyde

The Research & Development Agreement signed between ITI Scotland Ltd and the Strathclyde University of Glasgow dated 2nd and 8th December 2008 for the value of [redacted]. Work package 3 to identify novel binding sites for selected targets and novel protein-protein interaction sites.

Part 4 Executed RDA Millipore Ltd

The Research & Development Agreement signed between ITI Scotland Ltd and the University of Glasgow dated the 10th February 2009 for the value of [redacted] Work package 5 to deliver a portfolio of 15 ubiquitin E3 ligases and validated high-throughput compatible assays.

Part 5 Executed Assignment from Mount Sinai

The Assignment of the patent "Targeted ubiquitination of proteins and screening methods using a new class of ubiquitin ligase proteins" Serial No. 11/685,122 filed March 12, 2007. Assignation signed on the 9th and 23rd March 2009.

Part 6 Representative list of Assigned IP

Reports, including but not limited to: Market and technology assessment reports, Target validation documents, Market research reports, Literature assessment reports and Commercial competition reports

Tools and Reagents, including but not limited to:

1. Purified proteins and substrates

For each of the primary targets, multiple tagged (HA, Myc, His) versions of each component of the E3 ligase complex have been cloned, expressed and purified. These have subsequently been assembled into active E3 ligase complexes. Similarly, multiple tagged versions of E1, an array of E2 enzymes and multiple physiologically relevant substrates of each E3 ligase have also been cloned, expressed and purified. In a number of cases, large amounts of these proteins have been expressed and purified to crystal grade purity for use in co-crystallisation trials with the identified E3 ligase modulator compounds

2. Biochemical assays

Functional high throughput compatible (96 and 384 well) biochemical assays for measuring the activity of the primary E3 ligase targets, as well as their associated enzyme cascades, have been

generated using optimised combinations of the above tagged proteins and substrates. The assays have been optimised to industrial standards (z', %CV) using several industry standard read-outs, including fluorescence polarisation (FP), time-resolved fluorescence (TR-FRET and HTRF) and enhanced chemiluminescence (ECL). Full standard operating procedures have been documented and patent applications filed (see section 5).

3. Biophysical assays

Biophysical assays for investigating the binding properties and the effects hit molecules have on the structure of E3 ligases have also been developed and optimised. These include Thermal Denaturation Fluorescence (TDF) assays which monitor the temperature at which the target melts and can discriminate between a false positive and a true ligand-type inhibitor and Surface Plasmon Resonance (SPR) which is an extremely sensitive method of detecting ligand binding. As well as binding, the stoichiometry and on/off rates can also be determined, enabling good discrimination between true ligand-type inhibitors and false positives

All to the extent that these tools and reagents do not fall under the technology obtained under the Licence executed on the same date as this Agreement

Platform Technologies:

1. Cell based assays

Cell based assays have been developed and optimized for the priority E3 ligase targets. The different assays have been used to demonstrate inhibition of the specific target within a relevant cellular environment and to confirm the potential role of inhibiting the target in ameliorating disease in physiologically relevant cellular models of disease. Two different cell based assay methodologies have been developed for each E3 ligase target. The first, directly measures the accumulation of endogenous levels of cellular substrates of the specific E3 ligase in tumour cell lines. The second system incorporates a fluorescent-based reporter system in which stable cell lines have been generated that incorporate fluorescent tagged versions of the target substrate. Control cell lines have also been generated that have mutated forms of the target binding site thus ensuring any effect of compounds is due to inhibition of the specific E3 ligase target and not off-target effects. Thus, in both systems, if the E3 ligase is inhibited, the levels of the specific substrate increase in the cells. Whilst specific for the priority E3 ligase targets, these platforms can be adapted for use for other E3 ligases.

2. Novel technology platforms for identifying modulators of E3 ligases

One of the key findings of the pre-programme scoping work was that traditional high throughput screening methodologies have generally failed to identify specific E3 ligase modulators; hence one of the key objectives of the programme was to develop technologies that enable the discovery of chemical or biological modulators of validated E3 ligase targets. With this in mind, two distinct platform technologies have been developed within the UPS programme to aid the identification of novel chemical modulators of E3 ligases.

The CODASS™ (COmbining Docking and Similarity Search) approach provides a novel platform technology for identifying and selecting potential hits for any target for which there is a crystal or NMR structure available. It is particularly well suited to studying protein-protein interaction interfaces such as those involved in E3 ligase: substrate interactions and E3 ligase complex formation. It provides an accurate enrichment of compounds to be further tested in functional biochemical assays with an unusually high percentage translation from predicted actives to verified functional hits. Typically 10-40% of all compounds identified by CODASS do show activity in subsequent functional assays. The process is also very rapid such that five million compounds and twenty five million conformers can be screened within two days. CODASS™ has been used to identify chemical modulators of three distinct E3 ligases. It has also been successfully used to identify active molecules against six different non-UPS targets. The CODASS™ platform is currently in the process of being protected (see section 5).

Similarly the PEPTIMIME™ platform technology is applicable to identifying peptidomimetic compounds for disrupting any protein-protein interactions that are directed via short sequences that do not involve tertiary structure. This is therefore applicable across all E3 ligases and other difficult to drug non-UPS targets. PEPTIMIME™ is a technology comprising a combination of domain mapping

and intelligent chemical substitution which facilitates discovery of novel disruptors of specific protein-protein interactions optimized for target selectivity, potency and stability. This approach has been used successfully to identify multiple low nanomolar E3 ligase inhibitors. Previous versions of PEPTIMIME™ have also been used to identify disruptors of >20 targets in multiple disease indications.

Hit/Lead Compounds:

Using the above technologies and functional assays hit compounds have been identified that demonstrate specific modulation of three E3 ligase targets. In the case of the priority target, these assays have enabled multiple rounds of design to drive potency 1000-fold within seven months to the point at which ten compounds have been identified that have IC50 values <10nM in the biochemical assays. These compounds also show no cross reactivity with other E3 ligases.