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ADDENDUM N°3 TO THE AGREEMENT

Between:

- **ERYTECH Pharma, S.A.** with a share capital of 792 461,10 euros €, having its registered head office in Lyon 08, Bâtiment Adénine, 60 avenue Rockefeller, registered with the Trade and Companies Registry of Lyon under the number 479 560 013, represented by Mr Gil BEYEN, Chief Executive Officer, (“**ERYTECH**”)
- and
- **ORPHAN EUROPE, S.A.R.L.**, with share capital of 320,000 €, having its registered head office in Puteaux, Immeuble Le Wilson, 70 Avenue du Général de Gaulle, registered with the Trade and Companies Registry of Nanterre under number 379 088 115, represented by Mr Andrea Recordati, Managing Director and Mr Massimo Mineo, General Manager EMEA (“**OE**”)

PREAMBLE

On 22 November 2012 ERYTECH and OE signed a License and Distribution Agreement (hereinafter referred to as the “**Agreement**”), according to which, amongst others, ERYTECH appointed OE as its exclusive distributor of the Product for the Primary Indications in the Territory and granted OE a license to the Licensed IP and the Trade Mark.

ERYTECH is finalizing with Medac GmbH some amendments to the Medac Agreements, concerning the supply of the L-asparaginase (native or recombinant, as the case may be) for the Product and the related supply price, as well as the term of the Medac Agreements. The execution versions of the addenda, respectively, to the 2008 Medac Agreement and to the 2011 Medac Agreement are attached hereto (the “**Medac Addenda**”).

In consideration of the above and of the terms of the Medac Addenda, ERYTECH and OE wish to amend the Agreement in order to adjust their contractual relationship to the new terms of the Medac Agreements.

IN CONSIDERATION OF THE MUTUAL COVENANTS EXPRESSED HEREIN, WHICH ARE INTEGRAL AND ESSENTIAL PART OF THIS ADDENDUM, THE PARTIES HERETO AGREE AS FOLLOWS:

A) If not otherwise specified in this Addendum, capitalized terms shall have the meaning attributed to them in the Agreement.

B) Subject to the terms hereof and to the execution of the Medac Addenda, pursuant to Art. 17.1 (O), OE [***].

Any proposal by ERYTECH to [***] shall be subject to a [***], unless [***] is required by Applicable Laws. It is understood that [***], having in mind its interest in marketing the Product, and maximizing its margin from such marketing, under the Agreement.

It is also agreed that ERYTECH shall bear all costs and expenses [***] (including, by way of example, costs and expenses for [***]).

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C) The Parties agree that the price for the supply of a [***] of [***] of [***] (being an item of the "[***]" under paragraph (i) of the "Supply Price" calculation in Schedule 1.1.4. to the Agreement), in the form of [***] and delivered to ERYTECH according to the 2011 Medac Agreement (as amended and integrated from time to time), (the "**Medac Product**") shall be charged by ERYTECH (as duly documented by ERYTECH) to OE at [***].

The Parties agree that [***] the price to be charged by ERYTECH to OE (as an item of the "[***]" under paragraph (i) of the "Supply Price" calculation in Schedule 1.1.4. to the Agreement) shall [***]; therefore, [***] and [***] shall be [***] by [***].

D) As a consequence of point C) above:

- (i) [***] (being an item of "[***]" under such definition/calculation of "Supply Price" as per Schedule 1.1.4 to the Agreement) according to point C) above and to reflect the above described mechanism; and
- (ii) Schedule 1.1.4 (Cost items in the Supply Price calculation) of the Agreement shall be cancelled and replaced with the new Schedule 1.1.4 attached to this Addendum; and
- (iii) [***] on the [***] shall be [***] according to the provisions of this Addendum.

E) Art. 17.5 and 17.6 of the Agreement are hereby deleted and cancelled.

F) Schedule 1.1.3 (List of Patents in Licensed IP) of the Agreement is updated as per Schedule F to this Addendum.

G) The definition of Territory is amended as follows: shall mean the 28 countries currently forming the European Union, Norway, Switzerland, Liechtenstein, Iceland, Serbia, Macedonia, Montenegro, Kosovo, Albania, and Bosnia and Herzegovina, including their current possessions and territories. In case a country currently member of the European Union is no longer a member of the European Union, it is understood that such country shall be in any case considered a country of the Territory.

H) This Addendum, including the related attachments, is essential and integral part of the Agreement. Except as expressly set forth by this Addendum, all terms and conditions of the Agreement as amended shall remain unchanged and in full force and effect.

In two originals,

For **ERYTECH**

On : 07 / 07 / 2016

/s/ Gil Beyen

Mr Gil BEYEN

Chief Executive Officer

For **OE**

On : 21 / 07 / 2016

Execution version

/s/ Andrea Recordati

Mr Andrea Recordati

Gérant/Managing Director

/s/ Massimo Mineo

Mr Massimo Mineo

General Manager EMEA

Execution version

SCHEDULE B): Execution versions of the addenda to the Medac Agreements

A) Execution version of Addendum 2 to the 2008 Medac Agreement

**ADDENDUM N° 2 TO
EXCLUSIVE SUPPLY AGREEMENT
for L-Asparaginase**

This Addendum is entered between:

ERYTECH Pharma S.A., a company incorporated under the laws of the Republic of France (n° 479 560 013 RCS Lyon; VAT No. FR 10479560013)), having its registered head office at Bâtiment Adenine, 60 avenue Rockefeller, 69008 Lyon, France, represented by Mr Gil Beyen, Chief Executive Officer, and by Mr Jérôme Bailly, Qualified Person,

hereinafter referred to as “**ERYTECH Pharma**”.

And,

medac GmbH, a company having its registered head office at Theaterstrasse 6, D22880 Wedel, Germany represented by Mr Nikolaus Graf Stolberg, Managing Director and Dr. Michaela Rehberg, Director Drug Regulatory Affairs (VAT No. DE 118579535)

hereinafter referred to as “**Medac**”.

hereinafter referred to individually or collectively as the “Parties” and individually as a “Party”.

WHEREAS

The Parties have signed an Exclusive Supply Agreement on 12th December 2008, as amended by virtue of Addendum 1 executed on 19th August 2009, (hereinafter “**the Agreement**”).

The Parties agree to modify certain Articles of the Agreement.

Therefore, the Agreement is hereby amended to read as follows:

- 1) The exclusivity of supply set forth in Section 3.1 of the Agreement shall be converted into non-exclusivity.
- 2) Section 4.3 of the Agreement shall be null and void.
- 3) Section 15.1 of the Agreement shall be null and void and replaced by the following:

“15.1. Term.

The term of this Agreement shall commence upon the Effective Date (i.e. 10th December 2008) and unless terminated earlier or extended pursuant to this Agreement shall expire twenty (20) years thereafter (i.e. 10th December 2028).

It is agreed between the Parties that in the event that after December 31, 2017, Medac's supplier of the Product discontinues in full the production of the Product for supplies to medac for the EU countries, the Agreement is suspended, including all rights and obligations of the Parties. This means that neither Party may claim or be liable for any contractual rights and/or obligations accordingly (with exception to Article XI. Confidentiality, Article XIII. Indemnification and Article XIV. Insurance).

It is understood between the Parties that in case the circumstance under the proceeding sentence occurs, Medac will not be deemed liable for the lack of supply of the Product to ERYTECH Pharma according to the Agreement and ERYTECH Pharma shall not be entitled to claim any compensation, direct, indirect, incidental or

consequential losses or damages howsoever caused, and whether based on warranty, contract, tort including negligence, strict liability or otherwise from Medac.

- 4) Section 15.2 of the Agreement shall be amended as follows:

“15.2. b):

[...]. Such possibility of termination does not exist in case of suspension of the Agreement according to Article 15.1. second paragraph of the Agreement.

“15.2. c):

After December 31, 2017, without notice and compensation by Medac in case (a) the European Commission definitely denies the current marketing authorisation application for GRASPA® (EMA/H/C/004055) (the “MAA”), (b) ERYtech withdraws the MAA or (c) ERYtech changes the MAA from using the Product to recombinant L-Asparaginase and obtains the marketing authorization relating to the changed MAA.

- 5) Section 15.3 first paragraph of the Agreement shall be null and void and replaced by the following:

“15.3. Consequences of Termination

Except with respect to a termination by Medac pursuant to Section 15.2. b), the expiration or termination of this Agreement will not relieve Medac from its obligation to provide with any Product to be delivered prior to the effective date of such expiration or termination.”

- 6) Except as otherwise provided herein, all terms and conditions of the Agreement shall remain in full force and effect and all terms beginning by a capitalized letter shall have the same meaning as those defined in the Agreement.

IN WITNESS whereof, the Parties have caused this Addendum to be executed by their duly authorized officers.

ERYTECH Pharma

Mr Gil Beyen
Chief Executive Officer

Place and date:

Lyon, July 5th, 2016

/s/ Gil Beyen

Signature

ERYTECH Pharma

Mr Jérôme Bailly
Qualified Person

Place and date:

Lyon, July 5th, 2016

/s/ Jérôme Bailly

Signature

Medac

Mr Nikolaus Graf Stolberg
Managing Director

Place and date:

Hamburg, July 15th, 2016

/s/ Nikolaus Graf Stolberg

Signature

Medac

ppa. Dr. Michaela Rehberg
Director Drug Regulatory Affairs

Place and date:

Hamburg, July 25th, 2016

/s/ Dr. Michaela Rehberg

Signature

B) Execution version of Addendum 2 to the 2011 Medac Agreement

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**ADDENDUM N° 2 TO
EXCLUSIVE SUPPLY AGREEMENT
for recombinant L-Asparaginase**

This Addendum is entered between:

ERYTECH Pharma S.A., a company incorporated under the laws of the Republic of France (n° 479 560 013 RCS Lyon; VAT No. FR 10479560013)), having its registered head office at Bâtiment Adenine, 60 avenue Rockefeller, 69008 Lyon, France, represented by Mr Gil Beyen, Chief Executive Officer, and by Mr Jérôme Bailly, Qualified Person,

hereinafter referred to as “**ERYTECH Pharma**”.
And,

medac GmbH, a company having its registered head office at Theaterstrasse 6, D22880 Wedel, Germany represented by Mr Nikolaus Graf Stolberg, Managing Director and Dr. Michaela Rehberg, Director Drug Regulatory Affairs (VAT No. DE 118579535)

hereinafter referred to as “**medac**”.

hereinafter referred to individually or collectively as the “Parties” and individually as a “Party”.

WHEREAS

The Parties have signed an Exclusive Supply Agreement on 3rd May 2011, as amended by virtue of Addendum 1 executed on 4th April 2014, (hereinafter “**the Agreement**”).

The Parties agree to modify certain Articles of the Agreement.

Therefore, the Agreement is hereby amended to read as follows:

- 1) From the date of signature of this Addendum, for the avoidance of doubt, the term “GRASPA®”, which for purposes of the Agreement, designates the medicinal product consisting in suspension of erythrocytes encapsulating recombinant L-asparaginase and released by ERYTECH Pharma, shall also include the medicinal product, internally designated as eryasp, consisting in suspension of erythrocytes encapsulating recombinant L-asparaginase and released by ERYTECH Pharma, which may not be commercialized under the “GRASPA®” trademark.
- 2) The exclusivity obligation under Section 3.1 of the Agreement (as well as any reference to such exclusivity obligation in the Agreement) shall be in force for five years from the first supply of the Product for commercial purposes.
- 3) Section 3.3 of the Agreement shall be null and void and replaced by the following:

3.3 Forecast

- ERYTECH Pharma shall provide medac with a rolling forecast of the quantities to be purchased over the next [***] (“Forecast”) of which the first [***] shall be made of quarterly projections, while the subsequent [***] shall be made of annual projections.

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- 4) Sections 4.1.1 and 4.1.2. of the Agreement shall be null and void and replaced by the following:

“4.1. Supply price of the Product

The price of the Product will be according to the following table:

Order volumes	Price per Product/ Euro
[***] batch	[***]
[***] batch	[***]
[***] batches ([***] campaign per year which will run from first Firm Order (“Commercial Year”))	[***]
[***] batches ([***] campaigns of [***] batches per Commercial Year)	[***]
[***] batches ([***] campaigns of [***] batches per Commercial Year)	[***]

It is agreed that each batch comprises a number of Products between around [***] and around [***].”

- 5) Section V of the Agreement shall be null and void and replaced by the following:

Article V. MUTUAL CONSENT

“[***].”

- 6) Section 7.1 of the Agreement shall be null and void and replaced by the following:

“7.1. Shipment.

Except as set out in Article 3.6 hereof and as long as the purchase orders made by ERYTECH Pharma are in compliance with the Forecast as defined under Article 3.3 hereof, medac shall ship, directly or through any Third Party, the Product to ERYTECH Pharma to one (1) delivery destination(s) in the European Union (in case of purchase order for commercial purposes) and any delivery destinations in the European Union (in case of purchase order for clinical purposes) specified in ERYTECH Pharma’s purchase orders within the lead-times described below, each of which will run, following the Firm Order:

- (i) [***] for [***] batch, if [***]

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(ii) [***] in case of [***] batch, if [***]

(iii) [***] in case of [***] to [***] batches ([***] to [***] campaigns of [***] batches each) per [***], if [***]

(iv) [***] in case of minimum [***] batches per Commercial Year, if [***]

Pursuant to shipment of at least [***] batch, Medac shall deliver Products with [***] of the Product.

[***].

7) Section 16.1 of the Agreement shall be cancelled and replaced with the following:

“16.1. Term and termination

The term of this Agreement shall commence upon the Effective Date and shall expire on 11th December 2028.

It is understood that save for the case of Force Majeure, only following the expiration of the exclusivity period of five years as per Section 3.1 of this Agreement and only in the event that medac's supplier of the API discontinues in full the production of the API and medac, therefore, becomes unable to supply the Product to ERYTECH Pharma, medac will be entitled to terminate the Agreement, by sending ERYTECH Pharma a 5-years prior written notice. For the avoidance of doubt, during this 5-years notice period, medac shall remain committed to ensure continuous supply of the Product in accordance with this Agreement.”

8) Section 16.2 shall be cancelled and replaced with the following:

“16.2 Termination. The Agreement may be terminated:

a) without notice and compensation by the mutual written agreement of the Parties; and

b) by either Party in the event a Party is in material default of the terms and conditions of this Agreement and fails to remedy the material default within one hundred twenty (120) days after receiving written notice specifying such default.”

9) Section XVIII below shall be added to the Agreement:

Article XVIII. RIGHT OF NEGOTIATION

medac, on its behalf and on behalf of its Affiliates acknowledges, it has been informed and understood that:

- as at the signature date of this Addendum, ERYTECH has granted to a partner with right to assign to [***] affiliates (hereinafter the “**Partner**”):
 - distribution and license rights with respect to a product developed by ERYTECH Pharma consisting of suspension of erythrocytes encapsulating L-Asparaginase:
 - in the 28 countries currently forming the European Union, [***]; and
 - for the ALL indication and the AML indication
 - a right of first negotiation notably in some additional territories, such as [***].
- In case of discrepancies between, the provisions of this Article 18 and any applicable provisions between the Partner and ERYTECH with respect to the rights granted as set out above, the provisions of this Article 18 will be modified automatically to the extent necessary to reflect what was agreed by the Partner and ERYTECH Pharma. ERYTECH Pharma shall notify medac of such modifications in writing.

[**]= CONFIDENTIAL TREATMENT REQUESTED

For the sole purpose of this Section, medac agrees and accepts that ERYTECH may disclose the existence of the following sections to Third Parties.

18.1. Right of first negotiation

In the event that within [**] of the date of this Addendum:

- ERYTECH Pharma is no longer bound by the distribution and license rights granted to the Partner and
- ERYTECH Pharma intends to enter into a license or other distribution arrangement with respect to GRASPA with any Third Party in relation to:
 - the 28 countries currently forming the European Union, [**] (hereinafter referred to as “Territories”); and in
 - the ALL indication and/or the AML indication (hereinafter referred to as “Indications”);

ERYTECH Pharma shall notify medac of such intention in writing without undue delay.

18.2. Right of second negotiation

In the event that within [**] of the date of this Addendum:

- ERYTECH Pharma intends to enter into a license or other distribution arrangement with respect to GRASPA with any Third Party besides the Partner in relation to:
 - Turkey, Russia [**] (hereinafter referred to as “Additional Territories”); and to
 - the Indications,
- and the Partner notifies ERYTECH Pharma that it does not wish to enter into discussions in relation to a license or other arrangement for such Additional Territories or Indications, or in the absence of any notification by the Partner within a period mutually agreed by ERYTECH Pharma and the Partner, or if ERYTECH Pharma is no longer bound by the right of first negotiation with the Partner;

ERYTECH Pharma shall notify medac of such intention in writing without undue delay.

18.3. Negotiation’s proceedings

Within [**] of ERYTECH Pharma’s notice to medac (within [**] if the notice falls in [**] or [**]), medac shall notify ERYTECH Pharma in writing whether it wishes to enter into discussions in relation to a license or other distribution arrangement with ERYTECH Pharma for the Territories, Additional Territories and Indications for which medac has a right of first negotiation or second negotiation in accordance with Sections 18.1 and 18.2. If medac notifies ERYTECH Pharma that it does not wish to enter into discussions in relation to a license or other distribution arrangement for such Territories, Additional Territories and Indications, or in the absence of any notification by medac within such period, ERYTECH Pharma shall be entitled to enter into a license or other distribution arrangement in relation to such Territories, Additional Territories and Indications with a Third Party.

If medac notifies ERYTECH Pharma that it wishes to enter into discussions in relation to a license or other distribution arrangement for such Territories, Additional Territories and indications the Parties shall negotiate exclusively in relation to the same for a period of [**] from the response of medac.

If the Parties have not entered into a definitive agreement in relation to such Territories, Additional Territories and Indications within the [***] period, ERYTECH Pharma shall be entitled to enter into a license or other distribution arrangement in relation to such Territories, Additional Territories and Indications with a Third Party provided that the [***].

[***] = CONFIDENTIAL TREATMENT REQUESTED

18.4 Right of information

Without prejudice to the right of first negotiation of the Partner as described above, in the event that within [***] of the date of this Addendum:

- ERYTECH intends to enter into a license or other distribution arrangement with respect to GRASPA with any Third Party in relation to:
 - countries where medac proves to be conducting significant distribution activities. Such countries are listed in Exhibit 4 and should be amended as the case may be by mutual agreement of the Parties; and to
 - the Indications,

ERYTECH undertakes to inform medac of such intention in writing without undue delay. If within [***] of ERYTECH Pharma's notice to medac (within [***] if the notice falls in [***] or [***]), medac notifies ERYTECH Pharma that it wishes to make an offer in relation to a license or other distribution arrangement for such countries and Indications, ERYTECH Pharma shall consider such offer in good faith but ERYTECH Pharma shall be free to enter into such license or other distribution arrangement with any Third Party.

10) Section XIX below shall be added to the Agreement:

“Article XIX: MUTUAL EFFORTS

medac hereby authorises ERYTECH Pharma to use the information and documents related to the recombinant L-asparaginase, already provided to ERYTECH Pharma in connection with the GRASPA® registration in ALL.

Without prejudice to the above, medac shall provide within a reasonable time and free of charge, ERYTECH Pharma with assistance and all the information/documents related to the recombinant L-asparaginase available at medac and not being under confidentiality obligations towards third parties and necessary to obtain the marketing authorization of the product developed by ERYTECH Pharma consisting of [***]. ERYTECH Pharma shall use reasonable commercial efforts to avoid any direct harm to medac.

If the documents/information to be provided by medac according to the preceding sentence are under confidentiality obligations towards third parties, medac shall make reasonable efforts to obtain disclosure of said documents or information from such third parties.

Without prejudice to the provisions of the Agreement as amended by this Addendum, ERYTECH Pharma shall [***].”

11) In case medac wishes to carry out investment to improve the manufacturing capacity for the Product, the Parties shall promptly inform each other and send the other Party a prospectus outlining the type of investment medac intends to make, and related costs and timeframes. Then, the Parties will discuss a possible cooperation and cost sharing, which shall not be unreasonably withheld by the Parties.

12) Except as otherwise provided herein, all terms and conditions of the Agreement shall remain in full force and effect and all terms beginning by a capitalized letter shall have the same meaning as those defined in the Agreement and in the Addendum n°1.

IN WITNESS whereof, the Parties have caused this Addendum to be executed by their duly authorized officers.

ERYTECH Pharma

Mr Gil Beyen
Chief Executive Officer

Place and date:
Lyon, July 5th, 2016

/s/ Gil Beyen

Signature

ERYTECH Pharma

Mr Jérôme Bailly
Qualified Person

Place and date:
Lyon, July 5th, 2016

/s/ Jérôme Bailly

Signature

Medac

Mr Nikolaus Graf Stolberg
Managing Director

Place and date:
Hamburg, 15.7.16

/s/ Nikolaus Graf Stolberg

Signature

Medac

ppa. Dr. Michaela Rehberg
Director Drug Regulatory Affairs

Place and date:
Hamburg, 25.07.16

/s/ Michaela Rehberg

Signature

[*] = CONFIDENTIAL TREATMENT REQUESTED**

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SCHEDULE F: Update of SCHEDULE 1.1.3 of the Agreement (List of Patents in Licensed IP)

[*]**

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SCHEDULE 1.1.4: Cost items in the Supply Price calculation

[***]