

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
22-505

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 22505

SUPPL # N/A

HFD # 510

Trade Name Egrifta for Injection

Generic Name tesamorelin for injection

Applicant Name Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)

Approval Date, If Known November 10, 2010

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

Investigation #1

YES

Explain:

!

!

! NO

! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

=====

Name of person completing form: Jennifer Johnson

Title: Regulatory Project Manager

Date: November 3, 2010

Name of Office/Division Director signing form: Mary H. Parks. M.D.

Title: Director, Division of Metabolism and Endocrinology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JENNIFER L JOHNSON
11/10/2010

MARY H PARKS
11/12/2010

Department of Health and Human Services Food and Drug Administration PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT <i>For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use</i>	Form Approved: OMB No. 0910-0513 Expiration Date: 04/30/10 See OMB Statement on Page 3.
	NDA NUMBER 22-505
	NAME OF APPLICANT / NDA HOLDER Theratechnologies Inc.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
EGRIFTA

ACTIVE INGREDIENT(S) tesamorelin acetate	STRENGTH(S) 1.1 mg/vial
---	----------------------------

DOSAGE FORM
Sterile lyophilized powder for injection

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

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FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number 6,020,311	b. Issue Date of Patent February 1, 2000	c. Expiration Date of Patent May 26, 2015
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d. Name of Patent Owner Theratechnologies Inc.	Address (of Patent Owner) 2310 blvd. Alfred-Nobel	
	City/State Montreal / Quebec / Canada	
	ZIP Code H4S 2B4	FAX Number (if available)
	Telephone Number 514-336-7800	E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) Mitchel Berstein Darby & Darby	Address (of agent or representative named in 1.e.) 7 World Trade Center, 250 Greenwich Street	
	City/State New York / NY	
	ZIP Code 10007-0042	FAX Number (if available) 212 527-7701
	Telephone Number 212-527-7700	E-Mail Address (if available) mberstein@darbylaw.com

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? Yes No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? Yes No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

- 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

- 3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
- 3.2 Does the patent claim only an intermediate? Yes No
- 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

- 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

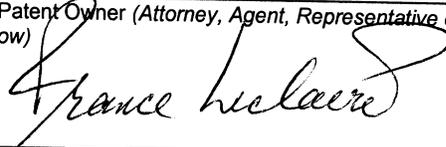
6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



Feb. 5, 2009

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
France Leclaire

Address
2310 blvd. Alfred-Nobel

City/State
Montreal / Quebec/ Canada

ZIP Code
H4S 2B4

Telephone Number
514-336-7800

FAX Number (if available)

E-Mail Address (if available)

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

**For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use**

NDA NUMBER

22-505

NAME OF APPLICANT / NDA HOLDER

Theratechnologies Inc.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

EGRIFTA

ACTIVE INGREDIENT(S)

tesamorelin acetate

STRENGTH(S)

1.1 mg /vial

DOSAGE FORM

Sterile lyophilized powder for injection

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).

Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

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FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

5,861,379

b. Issue Date of Patent

January 19, 1999

c. Expiration Date of Patent

May 26, 2015

d. Name of Patent Owner

Theratechnologies Inc.

Address (of Patent Owner)

2310 blvd. Alfred-Nobel

City/State

Montreal / Quebec / Canada

ZIP Code

H4S 2B4

FAX Number (if available)

Telephone Number

514-336-7800

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

 Mitchel Berstein
Darby & Darby

Address (of agent or representative named in 1.e.)

7 World Trade Center, 250 Greenwich Street

City/State

New York / NY

ZIP Code

10007-0042

FAX Number (if available)

212 527-7701

Telephone Number

212-527-7700

E-Mail Address (if available)

mberstein@darbylaw.com

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

- 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

- 3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
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4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

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Date Signed

France Leclaire

Feb 5, 2009

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NDA Applicant/Holder

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Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
France Leclaire

Address
2310 blvd. Alfred-Nobel

City/State
Montreal / Quebec /Canada

ZIP Code
H4S 2B4

Telephone Number
514-336-7800

FAX Number (if available)

E-Mail Address (if available)

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Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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**PATENT INFORMATION SUBMITTED WITH THE
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*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

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NAME OF APPLICANT / NDA HOLDER

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ACTIVE INGREDIENT(S)

tesamorelin acetate

STRENGTH(S)

1.1 mg/vial

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Sterile lyophilized powder for injection

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1. GENERAL

a. United States Patent Number

7,316,997

b. Issue Date of Patent

January 8, 2008

c. Expiration Date of Patent

May 29, 2023

d. Name of Patent Owner

Theratechnologies Inc.

Address (of Patent Owner)

2310 blvd. Alfred-Nobel

City/State

Montreal / Quebec / Canada

ZIP Code

H4S 2B4

FAX Number (if available)

Telephone Number

514-336-7800

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

 Mitchel Berstein
Darby & Darby

Address (of agent or representative named in 1.e.)

7 World Trade Center, 250 Greenwich Street

City/State

New York / NY

ZIP Code

10007-0042

FAX Number (if available)

212 527-7701

Telephone Number

212-527-7700

E-Mail Address (if available)

mberstein@darbylaw.com

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

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2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) Claims 1 to 8	Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
--	--

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.) EGRIFTA is indicated to induce and maintain a reduction of excess abdominal fat in HIV-infected patients with lipodystrophy.
---	--

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



Feb. 5, 2009.

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
France Leclaire.

Address
2310 blvd. Alfred-Nobel

City/State
Montreal / Quebec/ Canada

ZIP Code
H4S 2B4

Telephone Number
514-336-7800

FAX Number (if available)

E-Mail Address (if available)

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

1.3. Administrative Information

3. DEBARMENT CERTIFICATION

Theratechnologies Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.



Martine Ortega

Vice-President, Regulatory Affairs and
Compliance

Theratechnologies Inc.

25 Feb. 2009

Date



Michelle Wilson

US Agent:

Michelle Wilson PhD

Senior Regulatory Affairs Consultant

Kendle International Inc.

2-26-09

Date

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/s/

JENNIFER L JOHNSON
10/27/2010

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Monday, October 25, 2010 6:39 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22505: Egrifta Carton and Container Labeling Comments from DMEPA and CMC

Attachments: DMEPA and CMC Egrifta carton and container label comments.pdf

Dear Michelle,

Our reviewers in CMC and DMEPA (Division of Medication Error Prevention and Analysis) have reviewed the carton and container labels, including those most recently submitted via email on October 22, 2010:

- Vial label
- Medication Box (1 of 2)
- Injection Kit Box (2 of 2)

Please see the attached document containing their recommendations for revisions to these labels:



DMEPA and CMC
Egrifta carton a...

Let me know if you have any questions.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

NDA 22505: Egrifta (tesamorelin) for Injection
Carton and Container Labeling Comments
(DMEPA and CMC)

Container Label

1. Increase the size of the proprietary name (Egrifta) and the established name (tesamorelin) on the principal display panel of the container label. Per 21 CFR 201.10(i) pertaining to small labels, information can be removed from the principal display panel of the container label to allow for a more prominent presentation of the proprietary name and the established name.

Carton Labeling for Egrifta Medication Box (Box 1 of 2)

1. Increase the size of the proprietary name (Egrifta) and the established name (tesamorelin) on the Medication Box (Box 1 of 2) carton labeling. It is important that patients using this product readily identify each element of the Egrifta kit in order to prepare the required materials for reconstitution and administration. A more prominent presentation of the product name will help facilitate the accurate identification of the product, Egrifta (tesamorelin), during the administration process.
2. Revise “55 mg mannitol USP” to “50 mg mannitol USP”. This represents the amount of mannitol in the dose.
3. Revise the reconstitution statement to alert the patient that the reconstitution process requires the use of **TWO VIALS** of product to achieve a 2 mg dose. For example:

Must be reconstituted before administration using **TWO VIALS** of Egrifta to achieve the required **2 mg** dose.

4. Add a statement to the principal display panel of the Egrifta Medication Box 1 of 2 alerting the patient to refrigerate the medication box until use. We recommend:

Keep Egrifta Vials Refrigerated Until Reconstitution and Administration

Carton Labeling for Egrifta Injection Kit (Box 2 of 2)

1. Revise the Egrifta Injection Kit Box (Box 2 of 2) carton labeling by itemizing the box contents in a format that corresponds to each item contained inside the box, including a large and prominent presentation of the identifiers (A through E) for easy identification. For example:
 - a. Thirty (30) sterile 3 mL syringes mounted with individual reconstitution needles
 - b. Thirty (30) individual 1 ½” 18 gauge sterile reconstitution needles
 - c. (b) (4)

- d. Thirty (30) 10 mL bottles of sterile water for injection, USP
 - e. Patient Instructions
 2. Revise the labeling language displayed on each of the boxes included inside the Egrifita Injection Kit (Box 2 of 2) to correspond, verbatim, to the list (above) on the carton labeling, including a large and prominent presentation of the identifiers (A through E) for easy identification:
 - a. Thirty (30) sterile 3-cc syringes mounted with individual reconstitution needles
 - b. Thirty (30) individual 1 ½” 18 gauge sterile reconstitution needles
 - c. (b) (4)
 - d. Thirty (30) 10 mL bottles of Sterile Water for Injection, USP
 - e. Patient Instructions
 3. Revise the unit of measure presented as ‘cc’ for the thirty (30) syringes on the labeling of the Injection Kit Box 2 of 2 to the unit of measure ‘mL’. The ‘mL’ presentation corresponds to the unit of measure that appears on each syringe as well as the presentation in the product insert labeling. The unit of measure presentation should align consistently throughout Egrifita labeling to provide clarity to the patient during reconstitution and administration of the product and minimize confusion that could lead to wrong dose medication errors.
 4. Add a statement to the outer package labeling of the thirty (30) vials of Sterile Water, USP alerting the patient that each vial is for single-use administration only. Because each Egrifita dose requires only 2.2 mL of Sterile Water, and the Sterile Water vial volume is 10 mL, patients may assume that they can reuse vials for future doses. We are concerned that the reuse of vials could introduce opportunities for contamination of the Sterile Water that could lead to patient infections. Adding a warning statement to the labeling of the Sterile Water packaging will alert the patient before use. We recommend a statement such as:

“For Single-Use Only – Dispose of Unused Portion After Each Administration”

5. Decrease the size of the proprietary name (Egrifita) and the established name (tesamorelin) on the Egrifita Injection Kit Box 2 of 2 labeling. Post-marketing experience of products that are packaged in kits such as Egrifita that require dilution and/or reconstitution has shown that medication errors have occurred due to the inadvertent administration of the inactive ingredient rather than the actual drug product. The proprietary and established names on the carton labeling of the injection kit appear very large and prominent, creating the potential for confusion that could lead to the assumption that the vials included in this box (Sterile Water) are actually the active drug product. Decreasing the prominence of the proprietary and established names on the carton labeling of the Injection Box Kit could help minimize the potential for such confusion. We recommend increasing the size of the words “Injection Kit Box 2 of 2” while decreasing the size of the proprietary name (Egrifita) and established name (tesamorelin) so that the words “Injection Kit Box (Box 2 of 2)” are larger and appear more prominent.

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/s/

JENNIFER L JOHNSON
10/25/2010

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Monday, October 26, 2009 4:51 PM
To: 'wilson.michelle@kendle.com'
Subject: Egrifita NDA 22-505: Statistical Dataset Resubmission Request

Good afternoon Michelle,

Our statistical reviewers were unable to open ADLB and ADLB_DLW in the analysis datasets for LIPO-008. Please resubmit these electronic datasets as soon as possible. Let me know if you have any questions.

Many thanks,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

11/02/2009

Email request sent to sponsor on October 26, 2009 (on behalf of statistical reviewer request made on October 23, 2009)

REQUEST FOR CONSULTATION

TO (Office/Division): **Badrul Chowdhury and Sally Seymour,**
Division of Pulmonary, Allergy and Rheumatology
Products (DPARP)

FROM (Name, Office/Division, and Phone Number of Requestor):
Jennifer Johnson, Regulatory Project Manager, DMEP,
WO22 Rm 3114, (301) 796-2194

DATE October 27, 2010	IND NO. N/A	NDA NO. 22505	TYPE OF DOCUMENT Package insert	DATE OF DOCUMENT N/A
NAME OF DRUG Egrifta (tesamorelin) for Injection, 1 mg/vial		PRIORITY CONSIDERATION Priority	CLASSIFICATION OF DRUG GnRH analog	DESIRED COMPLETION DATE November 3, 2010

NAME OF FIRM: Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: Please review the attached documents pertaining to hypersensitivity reactions in the Egrifta drug development program and advise the Division on the appropriate labeling for these reactions. Let me know if you have any questions. We plan on taking an action on Egrifta on November 10th. The clinical reviewer for this application is Ali Mohamadi (clinical team leader: Dragos Roman). Many thanks, Jennifer

SIGNATURE OF REQUESTOR Jennifer Johnson	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

JENNIFER L JOHNSON
10/27/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (<i>Division/Office</i>): Enid Galliers – Supervisory Regulatory Project Manager Division of Metabolism and Endocrine Drug Products (DMEP)		FROM(<i>Division/Office</i>) Samuel M. Skariah – Regulatory Review Officer Division of Drug Marketing, Advertising and Communications (DDMAC)		
DATE: September 16, 2010	IND NO.	NDA NO. 022505	TYPE OF DOCUMENT: Promotional Material	DATE OF DOCUMENTS: September 3, 2010
NAME OF DRUG EGRIFTA™ (tesamorelin for injection)	PRIORITY CONSIDERATION YES	CLASSIFICATION OF DRUG: Growth Hormone Releasing Factor	DESIRED COMPLETION DATE: October 5, 2010	
NAME OF FIRM: Kendle International				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> LABELING REVISION <input checked="" type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> SAFETY <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> PAPER NDA <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> OTHER (<i>SPECIFY BELOW</i>): <input type="checkbox"/> MEETING PLANNED BY				
COMMENTS/SPECIAL INSTRUCTIONS: I am reviewing some launch promotional pieces for advisory comments. These pieces were submitted by Kendle International for Egrifta and are intended for healthcare professionals. I would appreciate the Review Division's input on several of the claims made in this piece. The consult request, the piece, and the references will be hand carried and delivered to your office. If you have any questions, I am located in Building 51, Room 3248 and can be reached at 301-796-2774. Thank you very much for your time.				
SIGNATURE OF REQUESTER		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL (DARRTS and email) <input type="checkbox"/> FACSIMILE		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

Date: September 16, 2010

From: Samuel M. Skariah – Regulatory Review Officer, DDMAC

To: Enid Galliers – Supervisory Regulatory Project Manager, DMEP

Re: Consult for DDMAC regarding Egrifta draft launch core visual aid and print advertisement directed to healthcare professionals (HCP)

I am reviewing a draft visual aid and HCP directed print advertisement for launch advisory comments. These pieces were submitted by Kendle International (Kendle) for Egrifta and are intended for HCPs. I would appreciate the Review Division's input on the following claims made in the piece.

[Redacted] (b) (4)

[Redacted]

2. [Redacted] (b) (4)

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

1 Lichtenstein KA. Redefining lipodystrophy syndrome: risks and impact on clinical decision making. *J Acquir Immune Defic Syndr.* 2005;39: 395-400

[Redacted]

[Redacted]

Please feel free to make any additional comments regarding other items in the pieces that appear misleading or problematic. Thank you very much for your time.

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/s/

SAMUEL M SKARIAH
09/16/2010

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Monday, September 13, 2010 5:51 PM
To: 'wilson.michelle@kendle.com'
Subject: Postmarketing Requirement (Microbiology)

Attachments: Micro PMR N22505.pdf

Dear Michelle,

As mentioned during our last teleconference, we are requesting a Postmarketing Requirement (PMR) per recommendation from our Microbiology reviewers. The rationale for this PMR is also shared by our reviewers in the Division of Medication Error Prevention Analysis (DMEP), in the Office of Surveillance and Epidemiology (OSE). Please see the attached document, and let me know if you have any questions.



Micro PMR
N22505.pdf (87 KB)

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Postmarketing Requirement (Microbiology) for Egrifta (tesamorelin) for Injection

On a post-approval, phase IV commitment basis, the sponsor must commit to studies for providing the daily dose (2 mg) of lyophilized product in a single vial. This single vial would replace the container-closure system described in the original application in which the daily dose is provided in two separate vials each containing 1.1 mg of lyophilized powder.

Study Objectives

The main goal of the studies will be to determine a process that allows for provision of a daily dose of lyophilized tesamorelin acetate product in a single vial. The process may involve replacing the current 3 mL, 13 mm, (b) (4) glass vial with an alternative vial. For all processes, testing shall be conducted using: (1) samples from three separate product batches; and (2) samples held under long term ($5^{\circ}\text{C} \pm 3^{\circ}\text{C}$) and accelerated ($25^{\circ}\text{C} \pm 3^{\circ}\text{C}$) storage conditions.

The sponsor is recommended to evaluate the results using the statistical guidelines described in: *Guidance for Industry – QIE Evaluation of Stability Data*.

Timeline

Studies and reporting shall be conducted according to the timeline presented below in Table 6 (page 2 of this document). As per this timeline:

- 1) Studies must be initiated no later than (NLT) one month following NDA approval.
- 2) No later than 15 months after NDA approval (14 months after study initiation) the sponsor must submit a *In Response to the Requirements for Phase IV Commitments* correspondence that summarizes stability data collected during the first year.
- 3) If a procedure for provision of the daily dose of drug product in a single vial is determined, the sponsor must submit no later than 31 months after NDA approval a supplement that proposes the use of this process for drug product manufacture. If a satisfactory process was not determined, the sponsor must submit a second *In Response to the Requirements for Phase IV Commitments* correspondence that summarizes the data and provides a justification for why provision of a daily dose of the product in a single container-closure is not feasible.

TABLE 6. Timeline for conducting single vial feasibility studies for Tesamorelin acetate

Time After NDA Approval	Time After Initiation of Stability Studies	Milestone
NLT 1 month	0 months	Feasibility studies initiated.
NLT 15 months	NLT 14 months	Sponsor submits a <i>In Response to the Requirements for Phase IV Commitments</i> correspondence that summarizes the results of studies conducted during the first year.
NLT 31 months	NLT 30 months	If a suitable process for providing the daily dose of the drug product in a single vial is determined, sponsor submits a supplement proposing manufacturing with this process. If a process is not found, the sponsor submits a second <i>In Response to the Requirements for Phase IV Commitments</i> correspondence that justifies why provision of the daily drug dose in a single single vial drug is not feasible.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON

09/13/2010

Micro PMR sent to sponsor via email on 9/13/10

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Thursday, August 26, 2010 2:21 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22505: Egrifta CMC Response to Thera Email Inquiries on August 13, 2010

Attachments: Thera Email to FDA v2 2010-08Aug-13.doc; CMC Label Response_081310.doc

Hi Michelle,

Please see the attached document for the CMC response to the questions from your August 13, 2010, email (also attached):



Thera Email to FDA
v2 2010-08A...



CMC Label
sponse_081310.doc

Let me know if you have any questions.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

5 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22505

ORIG-1

THERATECHNOLO
GIES INC

Egrifta

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/s/

JENNIFER L JOHNSON

08/26/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): CDER Pediatric and Maternal Health Staff, Maternal Health Team Attn: Tammie Brent Howard, (301) 796-1409		FROM: Jennifer Johnson, RPM, Division of Metabolism and Endocrinology Products, WO22 Rm 3114, (301) 796-2194		
DATE August 2, 2010	IND NO. N/A	NDA NO. 22505	TYPE OF DOCUMENT Original NDA (package insert)	DATE OF DOCUMENT N/A
NAME OF DRUG Egrifta (tesamorelin) for Injection, 1 mg/vial		PRIORITY CONSIDERATION Priority	CLASSIFICATION OF DRUG GnRH analog	DESIRED COMPLETION DATE August 20, 2010 or ASAP
NAME OF FIRM: Theratechnologies, Inc.				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Pregnancy Labeling review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS: Please review Section 8 (8.1 and 8.3) of the package insert for Egrifta, a new molecular entity. The NDA was submitted on May 29, 2009, and our current action goal date is September 29, 2010 (action package due to ODE II on September 8, 2010). Our review team has been working on revising the label, including edits by pharmacology/toxicology (primary reviewer = Lauren Murphree Mihalcik; supervisor = Todd Bourcier). The medical reviewer is Ali Mohamadi (clinical team leader and CDTL = Dragos Roman). The clinical pharmacology reviewer is Ritesh Jain (team leader = Sally Choe). Please see the most recent package insert in the DMEP eRoom via the following link: http://erom.fda.gov/eRoom/CDER3/CDERDivisionofMetabolismandEndocrinologyProductsConsults/0_17d2b				
Feel free to contact me with any questions. Many thanks, Jennifer				
SIGNATURE OF REQUESTER Jennifer Johnson		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DARRTS/EMAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON
08/02/2010

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Wednesday, June 23, 2010 3:59 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Post-marketing Requirements for Egrifta

Dear Michelle,

Following the May 27, 2010, Advisory Committee meeting, our review team is in the midst of finalizing reviews and discussing labeling and the risk management program for Egrifta. As such, we are considering the following two post-marketing required studies.

(b) (4)

- A randomized, controlled clinical trial to assess the benefit (or non-inferiority) of a reduction in VAT on cardiovascular outcomes (MACE). In designing your trial, please consider the input from the Advisory Committee, such that adequate numbers of women and racial sub-groups are enrolled. We also strongly encourage you to include subjects with diabetes. You should also plan on further assessing other safety endpoints in the trial, such as IGF-1 levels, malignancies, liver and/or kidney abnormalities, and in a subset of diabetic patients, retinopathy. Other endpoints (secondary or exploratory) of interest would be compliance with anti-retroviral therapy, quality of life (using an approved, validated PRO instrument), and perhaps pulmonary function and sleep apnea.

At this time we are asking that you submit a synopsis of a protocol for the clinical trial, and to provide timelines for both the embryofetal development study and the clinical trial. The timelines should include dates for Final Protocol Submission, Study Completion, and Final Study Report Submission. You should allow sufficient time in the Final Protocol Submission date such that the proposed protocol can be submitted, reviewed, commented on, and revised as needed to meet the study requirement as determined by the Division. We suggest 90 days from the date of submission of the initial protocol proposal.

Please let me know if you have any questions.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON

06/23/2010

Email to sponsor notifying of 2 studies to be required post-marketing

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Wednesday, June 16, 2010 12:49 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505 (Egrifta): Request for Information

Dear Michelle,

Could you please submit to the NDA a summary of the explanation that Dr. Cohen provided at the Advisory Committee on May 27, 2010, regarding the fact that the IGF-1 levels are expected to be different in HIV patients with lipodystrophy than in normal patients (i.e., more variability, a larger dataset than the one that resulted in the (b) (4) norms, etc)? We would just like to have all available data on file in the NDA.

Let me know if you have any questions. I am at the DIA conference this week but do check emails in the evenings.

Many thanks,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON

06/23/2010

Email request sent to sponsor on June 16, 2010

Johnson, Jennifer

From: Fong, Steven
Sent: Wednesday, June 09, 2010 1:03 PM
To: 'MWilson@Theratech.com'
Cc: Johnson, Jennifer
Subject: Micro IR for NDA 22-505/N-000

Follow Up Flag: Follow up
Due By: Thursday, June 10, 2010 1:00 AM
Flag Status: Red

Dear Dr. Wilson--

I am doing a microbiology review for NDA 22-505/N-000, and have a last minute information request. I would like to request that, as soon as possible, you provide an amendment response to the items presented below (in blue). Please e-mail the response directly to me as well as submitting to Global Submit.

Due to the Advisory Committee meeting for this application, the due date for reviews was delayed, but I need to have mine completed no later than early next week (Monday June 14th or Tuesday 15th). In the interest of time, I am submitting this IR directly to you as well as notifying the RPM, Jennifer Johnson.

Thanking you in advance.

Steve

Steven E. Fong, M.S., Ph.D.

Reviewer, New Drug Microbiology Staff
Office of Pharmaceutical Science/CDER
US Food and Drug Administration
10903 New Hampshire Avenue
Bldg 51, Room 4161
Silver Spring, MD 20993-0002
(301) 796-1501

- (1) Please provide 510K application numbers for the following Egrifita kit components. If this information is already in the application please indicate the location:
- a. 3 cc syringes equipped with 1-1/2" 18 gauge needles.
 - b. 1-1/2" 18 gauge needles (supplied separately from the 3 cc syringes)
[REDACTED] (b) (4)
 - d. 1/2" 27-gauge needles.

- (2) The draft labelling (item 16, page 18) includes the following statement: [REDACTED] (b) (4)

[REDACTED] (b) (4)

- (3) What is the volume of sterile water for injection, USP in the 10 mL plastic diluent vials provided with the Egrifita kit?

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON

06/10/2010

Email request sent to sponsor by microbiology reviewer on 6/9/10. Email response received from sponsor on 6/9/10; official response expected soon.

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO:
CDER-DDMAC-RPM
(c/o Sam Skariah/Kendra Jones/Paul Loebach)

FROM: (Name/Title, Office/Division/Phone number of requestor)
Jennifer Johnson, RPM
Division of Metabolism and Endocrinology Products
WO22 Rm 3114; 301-796-2194

REQUEST DATE
April 9, 2010

IND NO.
N/A

NDA/BLA NO.
22-505

TYPE OF DOCUMENTS
(PLEASE CHECK OFF BELOW)

NAME OF DRUG
Egrifta (tesamorelin acetate) for Injection, 1 mg/vial

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG
GnRH analog

DESIRED COMPLETION DATE
June 18, 2010

NAME OF FIRM:
Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)

PDUFA Date:
March 29, 2010 (new goal date: July 27, 2010)

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:
(Check all that apply)

- PACKAGE INSERT (PI)
- PATIENT PACKAGE INSERT (PPI)
- CARTON/CONTAINER LABELING
- MEDICATION GUIDE
- INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION

- ORIGINAL NDA/BLA
- IND
- EFFICACY SUPPLEMENT
- SAFETY SUPPLEMENT
- LABELING SUPPLEMENT
- PLR CONVERSION

REASON FOR LABELING CONSULT

- INITIAL PROPOSED LABELING
- LABELING REVISION

EDR links to relevant submissions:

Original application submitted May 29, 2009: <\\Cdsub1\evsprod\nda022505\0000>

Revised labeling submitted July 31, 2009: <\\Cdsub1\evsprod\nda022505\0005>

Revised labeling submitted (MedGuide) on December 17, 2009: <\\Cdsub1\evsprod\nda022505\0014>

Revised labeling submitted (MedGuide – Word) on January 20, 2010: <\\Cdsub1\evsprod\nda022505\0018>

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: October 16, 2009

Labeling Meetings: TBD

Wrap-Up Meeting: TBD

I will send additional details via email; it is not certain at this time whether this product will be approved.

Thanks, Jennifer

SIGNATURE OF REQUESTER
Jennifer Johnson

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)

eMAIL (DARRTS)

HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON
04/09/2010

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Wednesday, March 17, 2010 5:52 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Egrifta (Additional Data Requested)

Attachments: Additional tables March 17 2010.doc

Dear Michelle,

After further internal discussion, we have some additional information to request from Theratechnologies for Egrifta, NDA 22-505.

The following four tables (shells) are attached to collect further information for our safety evaluation, particularly for "completers" only (patients who had HbA1c and fasting blood glucose measured at all timepoints throughout the pivotal trials).



Additional tables
March 17 201...

Please let me know if you have any questions or concerns.

Thanks in advance for your help!

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

For the table below, please include ONLY “completers” – that is, patients who had HbA1c measured at ALL of the following timepoints: Weeks 0, 13, and 26. Please do not include patients who had HbA1c measured at “alternate” weeks (ie, week 19 instead of 26). Please exclude values obtained at “additional” weeks (if the patient had A1c drawn at Weeks 0, 13, 19, and 26, please disregard the Week 19 value).

Shifts in HbA1c – Main Phase of Pivotal Trials (Both Trials Combined, Completers Only)

Baseline Evaluation		Tesamorelin N=			Placebo N=		
		Post-Baseline Evaluation					
		Normal	Pre-Diabetes	DM	Normal	Pre-Diabetes	DM
Normal	Week 13						
	Week 26						
Pre-Diabetes	Week 13						
	Week 26						
DM	Week 13						
	Week 26						

Normal = A1c < 5.7%

Pre-Diabetes = 5.7% ≤ A1c < 6.5

DM = A1c ≥ 6.5%

For the table below, please include ONLY “completers” – that is, patients who had HbA1c measured at ALL of the following timepoints: start of the Extension Phase, Week 39, and Week 52. Please do not include patients who had HbA1c measured at “alternate” weeks (ie, week 45 instead of 52). Please exclude values obtained at “additional” weeks (if the patient had A1c drawn at start of Extension Phase, 39, 45, and 52, please disregard the Week 52 value).

Shifts in HbA1c – Extension Phase of Pivotal Trials (Both Trials Combined, Completers Only)

Baseline Evaluation		T-T N=			T-P N=		
		Post-Baseline Evaluation					
		Normal	Pre-Diabetes	DM	Normal	Pre-Diabetes	DM
Normal	Week 39						
	Week 52						
Pre-Diabetes	Week 39						
	Week 52						
DM	Week 39						
	Week 52						

Normal = A1c < 5.7%
 Pre-Diabetes = 5.7% ≤ A1c < 6.5
 DM = A1c ≥ 6.5%

For the table below, please include ONLY “completers” – that is, patients who had FBG measured at ALL of the following timepoints: Weeks 0, 6, 13, 19 and 26. Please do not include patients who had FBG measured at “alternate” weeks (ie, week 22 instead of 26). Please exclude values obtained at “additional” weeks (if the patient had FBG drawn at Weeks 0, 6, 13, 19, 22, and 26, please disregard the Week 22 value).

Table XX: Shifts in Glucose Tolerance – Main Phase of Pivotal Trials (Both Trials Combined, Completers Only)

		Tesamorelin N=			Placebo N=		
Baseline Evaluation		Post-Baseline Evaluation					
		Normal	IFG/IGT	DM	Normal	IFG/IGT	DM
Normal	Week 6						
	Week 13						
	Week 19						
	Week 26						
IFG/IGT	Week 6						
	Week 13						
	Week 19						
	Week 26						
DM	Week 6						
	Week 13						
	Week 19						
	Week 26						

Source: LIPO-010 Table 14.3.4.5.2c, LIPO-011 Table 14.3.4.5.2c
 Normal = FBG < 100 mg/dL, or OGTT < 140
 IGT = 100 mg/dL ≤ FBG ≤ 125, or 140 ≤ 2-hr OGTT ≤ 199
 DM = FBG > 125, or OGTT > 199

For the table below, please include ONLY “completers” – that is, patients who had FBG measured at ALL of the following timepoints: baseline for the Extension Phase, and weeks 32, 39, 45 and 52. Please do not include patients who had FBG measured at “alternate” weeks (ie, week 49 instead of 52). Please exclude values obtained at “additional” weeks (if the patient had FBG drawn at baseline and weeks 32, 39, 45, 49 and 52, please disregard the Week 52 value).

Table XX: Shifts in Glucose Tolerance – Extension Phase of Pivotal Trials (Both Trials Combined, Completers Only)

		T-T N=			T-P N=		
Baseline Evaluation		Post-Baseline Evaluation					
		Normal	IFG/IGT	DM	Normal	IFG/IGT	DM
Normal	Week 32						
	Week 39						
	Week 45						
	Week 52						
IFG/IGT	Week 32						
	Week 39						
	Week 45						
	Week 52						
DM	Week 32						
	Week 39						
	Week 45						
	Week 52						

Source: LIPO-010 Table 14.3.4.5.2c, LIPO-011 Table 14.3.4.5.2c

Normal = FBG < 100 mg/dL, or OGTT < 140

IGT = 100 mg/dL ≤ FBG ≤ 125, or 140 ≤ 2-hr OGTT ≤ 199

DM = FBG > 125, or OGTT > 199

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON

03/17/2010

Data request made by clinical reviewer Ali Mohamadi on 3/17/2010 (concurrence from Dragos Roman, clinical team leader)

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Thursday, March 11, 2010 5:31 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Egrifta (Requests for Information from Today's Teleconference)

Attachments: Safety tables Egrifta March 11 2010.doc

Dear Michelle,

Thank you again for your time during today's teleconference with Theratechnologies and FDA to address areas of concern related to safety.

As mentioned during our discussion, we are requesting the following:

1. Please provide data as detailed in the attached table shells for:
 - Hemoglobin A1c
 - Fasting Blood Glucose
 - IGF-1/Cancer Adverse Events



Safety tables
Egrifta March 11...

2. Provide a reference (or highlight its location in the application) explaining the admission criteria regarding abdominal circumference.
3. **Immunogenicity:** provide a summary description of the assay used in the pivotal studies, including a justification/argument for your approach.

As stated during the teleconference, it is acceptable to submit your responses to the NDA as soon they are ready (i.e., in piecemeal form); you do not have to wait until you have compiled all responses to our information requests before submitting them.

We will defer discussions regarding the REMS to a later date (TBD).

Let us know if you have any questions or concerns.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

I. Hemoglobin A1c Data

Proportion of Patients with Normal BG, Pre-Diabetes, or DM (based on HbA1c) – Main Phase of Pivotal Studies (Both Studies Combined)

	Status	Tesamorelin N=543 n (%)	Placebo N=263 n (%)
Baseline	Normal		
	Pre-Diabetes		
	DM		
Week 13	Normal		
	Pre-Diabetes		
	DM		
Week 26	Normal		
	Pre-Diabetes		
	DM		

Normal = A1c < 5.7%

Pre-Diabetes = 5.7% ≤ A1c < 6.5

DM = A1c ≥ 6.5%

Proportion of Patients with Normal BG, Pre-Diabetes, or DM (based on HbA1c) – Extension Phase of Pivotal Studies (Both Studies Combined)

	Status	T-T N=246 n (%)	T-P N=135 n (%)
Week 26	Normal		
	Pre-Diabetes		
	DM		
Week 39	Normal		
	Pre-Diabetes		
	DM		
Week 52	Normal		
	Pre-Diabetes		
	DM		

Normal = A1c < 5.7%

Pre-Diabetes = 5.7% ≤ A1c < 6.5

DM = A1c ≥ 6.5%

Shifts in HbA1c – Main Phase of Pivotal Trials (Both Trials Combined)

Baseline Evaluation		Tesamorelin N=543			Placebo N=263		
		Post-Baseline Evaluation					
		Normal	Pre-Diabetes	DM	Normal	Pre-Diabetes	DM
Normal	Week 13						
	Week 26						
Pre-Diabetes	Week 13						

	Week 26						
DM	Week 13						
	Week 26						

Normal = A1c < 5.7%
 Pre-Diabetes = 5.7% ≤ A1c < 6.5
 DM = A1c ≥ 6.5%

Shifts in HbA1c – Extension Phase of Pivotal Trials (Both Trials Combined)

Baseline Evaluation		T-T N=246			T-P N=135		
		Post-Baseline Evaluation					
		Normal	Pre-Diabetes	DM	Normal	Pre-Diabetes	DM
Normal	Week 39						
	Week 52						
Pre-Diabetes	Week 39						
	Week 52						
DM	Week 39						
	Week 52						

Normal = A1c < 5.7%
 Pre-Diabetes = 5.7% ≤ A1c < 6.5
 DM = A1c ≥ 6.5%

NOTE Re: Shifts (Next 2 tables):

A “shift” is considered movement into another HIGHER category compared the BASELINE value. Categories are defined below each table.

For example, a patient with a baseline HbA1c of 5.0% who has an HbA1c of 5.9% at Week 13 and 7.0% at week 26 is considered to have 1+1= **2 shifts**. (ie, a shift from “normal” to “DM” is considered one shift in this analysis. In contrast, a patient with an HbA1c of 5.5% at baseline, 5.9% at Week 13 and 5.0% at Week 36 is considered to have had 1+0= **1 shift**.

Shifts* in HbA1c – Main Phase of Pivotal Trials (Both Trials Combined)

Number of Shifts	Tesamorelin N=543	Placebo N=263
0		
1		
2		

*Defined as number of times patient had HbA1c in a higher category compared to baseline during Main Phase
 Category 1: HbA1c < 5.7%
 Category 2: 5.7% ≤ A1c < 6.5
 Category 3: HbA1c ≥ 6.5%

Shifts* in HbA1c – Extension Phase of Pivotal Trials (Both Trials Combined)

Number of Shifts	T-T N=246	T-P N=135
0		
1		
2		

*Defined as number of times patient had HbA1c in a higher category compared to baseline during Main Phase

Category 1: HbA1c < 5.7%

Category 2: 5.7% ≤ A1c < 6.5

Category 3: HbA1c ≥ 6.5%

HbA1c Trends: Individual Patients with At Least One Value ≥ 6.5% -- Main Phase of Pivotal Trials (Both Trials Combined)

	Patient ID	HbA1c (%)		
		Week 0	Week 13	Week 26
Tesamorelin				
Placebo				

HbA1c Trends: Individual Patients with At Least One Value ≥ 6.5% -- Extension Phase of Pivotal Trials (Both Trials Combined)

	Patient ID	HbA1c (%)		
		Week 26	Week 39	Week 52
T-T				
T-P				

II. FBG Data

Change in FBG From Baseline* to Week 52 – Extension Phase of Pivotal Studies (Both Studies Combined)

	T-T N=246			T-P N=135			
FBG (mg/dL)	N	Mean (SD)	Min, Max	N	Mean (SD)	Min, Max	P-value
Baseline							
Week 32							
Week 32: Change from Baseline							
Baseline	226	96.81 (13.02)	61.2, 153.9	117	101.79 (16.36)	75.9, 170.9	
Week 39	226	100.64 (13.26)	67.9, 171.0	118	99.76 (13.16)	76.9, 161.9	
Week 39: Change from Baseline	226	3.83 (16.27)		117	-2.04 (15.49)		????
Baseline							
Week 45							
Week 45: Change from Baseline							????
Baseline	201	97.11 (13.09)	61.2, 153.9	98	102.23 (16.86)	75.9, 170.9	
Week 52	202	98.95 (14.30)	68.4, 201.6	99	100.22 (28.45)	42.0, 330.7	
Week 52: Change from Baseline	201	1.87 (14.48)		98	-2.02 (28.24)		????

Source: ISS Table 1.5.2.2.10a

*Baseline: Latest non-missing available measurement prior to first dose of Extension Phase

NOTE Re: Shifts (Next 2 tables):

A “shift” is considered movement into another HIGHER category compared the BASELINE value. Categories are defined below each table.

For example, a patient with a baseline FBG of 99 mg/dL who has an FBG of 105 mg/dL at Week 6, 110 at Week 13, 95 at Week 19 and 150 at Week 26 is considered to have 1+1+0+1= **3 shifts**. (ie, a shift from “normal” to “DM” is considered one shift in this analysis. In contrast, a patient with an FBG of 95 at baseline, 90 at Week 6, 150 at Week 13, 90 at Week 19 and 90 at Week 26 is considered to have had 0+1+0+0=**1 shift**.

Shifts* in FBG – Main Phase of Pivotal Trials (Both Trials Combined)

Number of Shifts	Tesamorelin N=543	Placebo N=263
0		
1		
2		

≥3		
-----------	--	--

*Defined as number of times patient had FBG in a higher category compared to baseline during Main Phase
 Category 1: FBG<100 mg/dL
 Category 2: 100 mg/dL ≤ FBG ≤ 125
 Category 3: FBG > 125

Shifts* in FBG – Extension Phase of Pivotal Trials (Both Trials Combined)

Number of Shifts	T-T N=246	T-P N=135
0		
1		
2		
≥3		

*Defined as number of times patient had FBG in a higher category compared to baseline during Main Phase
 Category 1: FBG<100 mg/dL
 Category 2: 100 mg/dL ≤ FBG ≤ 125
 Category 3: FBG > 125

FBG Trends: Individual Patients with At Least One Value ≥ 126 mg/dL -- Main Phase of Pivotal Trials (Both Trials Combined)

		FBG (mg/dL)				
	Patient ID	Week 0	Week 6	Week 13	Week 19	Week 26
Tesamorelin						
Placebo						

FBG Trends: Individual Patients with At Least One Value ≥ 126 mg/dL -- Extension Phase of Pivotal Trials (Both Trials Combined)

		FBG (mg/dL)				
	Patient ID	Week 26	Week 32	Week 39	Week 45	Week 52
T-T						
T-P						

III. IGF-1/Cancer Data

Cancer Adverse Events – Pivotal and Non-Pivotal Trials

Study	Age/Gender	Treatment (dose)	Type of Cancer	Duration of Exposure (days)	Investigator's assessment (relationship to treatment)
Pivotal Studies: Main Phase					
10	60/M	Tesamorelin (2 mg/day)	Rectal cancer*	150	Unrelated
10	57/M	Tesamorelin (2 mg/day)	Basal cell carcinoma*	43	Unrelated
10 ⁺		Tesamorelin (2 mg/day)	Prostatic neoplasm		Unrelated
11 ⁺		Tesamorelin (2 mg/day)	Lung neoplasm		Unrelated
11 ⁺		Tesamorelin (2 mg/day)	Basal cell carcinoma		Unrelated
11	39/F	Placebo	Breast cancer in situ*	NA	Unrelated
11	40/M	Placebo	Hodgkin's disease*	NA	Related
11 ⁺		Placebo	Basal cell carcinoma		Unrelated
Pivotal Studies: Extension Phase					
10 ⁺		T-T	Basal cell carcinoma		Unrelated
10 ⁺		P-T	Basal cell carcinoma		Unrelated
10 ⁺		P-T	Kaposi's sarcoma		Unrelated
10 ⁺		P-T	Lung neoplasm		Unrelated
10 ⁺		T-P	Basal cell carcinoma		Unrelated
10	44/M	T-P	Anal cancer*	335	Unrelated
12	50/M	T-P	Hodgkin's disease*	436	Related [#]
Non-pivotal Studies					
004	84/F	Tesamorelin (2 mg/day)	Tracheal cancer*	27	Unrelated
007 ⁺		Tesamorelin (1 mg/day)	Prostatic neoplasm		Unrelated

Source: Summary of Clinical Safety Table 20

*Also reported as an SAE

[†]Narrative unavailable

[#]Investigator judged there was a possibility of causal relationship to placebo

T-T = tesamorelin 2 mg/day during Main Phase and tesamorelin during the Extension Phase.

P-T = placebo during Main Phase and tesamorelin 2 mg/day during the Extension Phase.

T-P = tesamorelin during Main Phase and placebo 2 mg/day during the Extension Phase.

IGF-1 Trends: Individual Patients with Cancer AEs -- Main Phase of Pivotal Trials (Both Trials Combined)

	Patient ID	Type of Cancer	IGF-1 (Value/SDS)		
			Week 0	Week 13	Week 26
Tesamorelin					
Placebo					

IGF-1 Trends: Individual Patients with Cancer AEs -- Extension Phase of Pivotal Trials (Both Trials Combined)

	IGF-1 (Value/SDS)				
	Patient ID	Type of Cancer	Week 27	Week 39	Week 52
T-T					
T-P					
P-T					

IGF-1 Trends: Individual Patients with Cancer AEs -- Extension Phase of Non-Pivotal Trials (Both Trials Combined)

	IGF-1 (Value/SDS)				
	Patient ID	Type of Cancer	Week XX	Week XX	Week XX
Tesamorelin					
Placebo					

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	Egrifta

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/s/

JENNIFER L JOHNSON

03/12/2010

Email sent to sponsor following teleconference on March 11, 2010 (requests made by Ali Mohamadi and Dragos Roman)

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Tuesday, January 12, 2010 2:59 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Egrifta Information Request (Updated Pediatric Plan)

Dear Michelle,

We have a request for an updated pediatric plan for postpubertal studies to be conducted with Egrifta, NDA 22-505. (Recall that this pediatric plan is a requirement for studies that are deferred under PREA. In your NDA application, you requested that studies be waived in prepubertal children and deferred for postpubertal children.)

Your pediatric plan, submitted on September 9, 2009, did not contain three required dates:

- A. Protocol Submission Date
- B. Study Start Date
- C. Final Report Submission Date

It is required that waiver requests/deferral requests/pediatric plans be reviewed by the Pediatric Review Committee (PeRC) prior to taking an action on applications. As this product is scheduled for review by PeRC on February 17, 2010, we will need for this revised pediatric plan to be submitted by **February 1, 2010**, including the three missing elements. PeRC will not review deferral requests without them.

Let me know if you have any questions.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22505

ORIG-1

THERATECHNOLO
GIES INC

Egrifta

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/s/

JENNIFER L JOHNSON

01/12/2010

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Friday, November 06, 2009 5:24 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Egrifta CMC Information Requests

Attachments: NDA 22505 CMC Info Request Nov 2009.doc

Dear Michelle,

We have some CMC requests for information - please see the attached document:



NDA 22505 CMC
Info Request Nov...

Please respond via an official amendment to NDA 22-505.
Let me know if you have any questions.

Thanks again for your help!

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

NDA 22-505

Egrifta™ (tesamorelin acetate for injection), 1 mg/vial

Chemistry, Manufacturing and Controls (CMC) Information Requests:

1. Identities of the peptide fragments represented by the peaks in the peptide map by LC/MS have not been provided as stated. Provide mapping results showing a) retention times, and b) peak areas for each fragment. In addition, provide mapping results comparing tesamorelin acetate lot FHEXGRF0401 with the reference material.
2. Provide a range for the number of acetate counter ions associated with each molecule of tesamorelin acetate.
3. Include an identity test for tesamorelin acetate using peptide mapping as part of the drug substance specifications. The peptide map of the sample tested must be identical to the peptide map of a reference material of liraglutide.
4. Provide a test for purity (area %) of tesamorelin acetate in the drug substance specifications including the test method and acceptance criteria.
5. Provide data from leachables studies on the (b) (4)
Guidance for these studies can be found in the FDA's Guidance for Industry, "Container Closure Systems for Packaging Human Drugs and Biologics", 1999.
6. Identify drug product batch(es) used in the Compatibility Studies described in Section 3.2.P.2 Pharmaceutical Development [tesamorelin, sterile lyophilized powder for injection, 1.1 mg/vial].
7. Include a test and acceptance criteria for bioidentity in the drug product specifications to adequately ensure bioactivity of tesamorelin acetate drug product.
8. Provide process validation results for each step in the manufacture of the drug product in order to demonstrate the capability to consistently produce tesamorelin acetate for injection according to the specified limits of the process parameters. It is claimed that three lots were validated for the bulk manufacture and filling of the drug product where all critical manufacturing and filling process parameters were monitored and all criteria were met. However, data to support this conclusion have not been provided. The tested parameters, acceptance criteria and results for a minimum of three drug product batches should be included. Results for the samples taken during the process validation, as well as in-process controls during both the start and end of the filling process, should be within the acceptance criteria for each of the three drug product batches evaluated.
9. Provide photostability testing results for tesamorelin acetate drug product in its primary packaging.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THE RATECHNOLOGIES INC	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

11/06/2009

CMC information requests sent to sponsor on behalf of CMC reviewer (request sent to RPM by reviewer via email on October 21, 2009)

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Thursday, November 05, 2009 4:39 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Egrifta - Request for Information (PRO Questionnaires)

Follow Up Flag: Follow up
Flag Status: Yellow

Good afternoon Michelle,

After review team discussion regarding the Patient Reported Outcomes (PRO) instrument used in the Phase 3 studies with Egrifta, we have determined that the case report forms included in the original NDA submission did not contain patient-related data and that a copy of the instrument administered to patients was not found in the case report forms.

Which forms did Theratechnologies use for the PRO studies? Are they the same as the blank PRO questionnaires contained in the DMF? We realize that you may not be able to answer these questions until you consult Phase V Technologies, since Theratechnologies does not have access to the DMF.

To aid in our review, please submit samples of the completed PRO questionnaires used at the study site(s), especially for these 3 endpoints: BAD (Belly Appearance Distress), BPA (Belly Profile Assessment) and BSE (Belly Size Estimation).

Please let me know if you have any questions.

Many thanks,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

(b) (4)

NDA-22505

ORIG-1

THERATECHNOLOGIES INC
TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

11/06/2009

Information request sent to sponsor via email on November 5, 2009 on behalf of clinical/SEALD/DSI reviewers

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Wednesday, October 07, 2009 6:16 PM
To: 'wilson.michelle@kendle.com'
Subject: Egrifta NDA 22-505: Request for Additional Datasets

Dear Michelle,

We have the following requests for additional datasets for Egrifta, NDA 22-505.

Regarding LIPO 010 (main phase and extension phase), and CTR 1011 (main phase) and CTR 1012 (extension phase):

1. Please construct a dataset for the primary efficacy endpoint (VAT), as well as all of the non-PRO-related secondary efficacy endpoints (e.g., trunk fat, abdominal SAT, total body fat, lean body mass, IGF-1, IGF-1 SDS, various lipids, etc), formatted like the ADIM dataset for the ISE. Also, in addition to variables for pre-treatment baseline (Day 0), and change and % change from pre-treatment baseline, please include variables for re-randomization baseline (at Week 26), change and % change from re-randomization baseline, country, pooled site, investigator name (initials), and number of days on study, and a flag for baseline carried forward data.

2. The PRO endpoints of primary interest are **belly** appearance distress (BAD), **belly** size estimation (BSE) and **belly** profile assessment (BPA). Please construct a dataset for BAD, BSE and BPA utilizing the same formatting requested in #1 above.

Please let me know if you have any questions regarding the above requests.

As always, thanks for your help.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES INC	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

10/08/2009

Clinical/statistical request for additional datasets sent to the sponsor via email on October 7, 2009

Johnson, Jennifer

From: Perlstein, Robert S
Sent: Monday, October 05, 2009 7:10 PM
To: 'wilson.michelle@kendle.com'
Cc: Roman, Dragos; Johnson, Jennifer
Subject: FW: 2009-09Sept-30 Perlstein Discussion 0007 v1
Importance: High

Michelle

I decided to formalize the additional questions that we discussed on the phone Friday morning. Please forward these questions to Theratech.

1. Approximately how many HIV+ patients are there in the USA in October 2009?
2. What are the state-of-the-art recommendations in October 2009 by AIDS authorities with regard to which HIV+ patients qualify for anti-retroviral therapy, i.e. history of an AIDS-defining infectious disease and/or malignancy, asymptomatic but T cell count less than X, asymptomatic but viral load in excess of Y, etc. Approximately what percentage (**and absolute number**) of the HIV+ population in the USA (**from question number 1**) are currently receiving anti-retroviral therapy?
3. Approximately what percentage (**and absolute number**) of the HIV+ patients currently receiving anti-retroviral therapy (**from question number 2**) have the lipodystrophy syndrome (central obesity [defined by gender-dependent waist circumference as in the inclusion criteria for your pivotal studies, **and predominantly due to increased abdominal VAT???**] and/or peripheral lipoatrophy) in the USA?
4. Amongst HIV+ patients currently receiving anti-retroviral therapy and diagnosed with lipodystrophy (**from question number 3**), approximately what percentage (**and absolute number**) have central obesity +/- lipoatrophy, and approximately what percentage (**and absolute number**) have lipoatrophy alone in the USA?
5. Am I correct in stating that the tens of millions centrally obese HIV- people in the USA have a much larger component of relatively **non-atherogenic** abdominal SAT than centrally obese HIV+ patients? Approximately what percentage of centrally obese HIV- people (defined by the gender-dependent waist circumference criteria listed in the diagnostic criteria for the metabolic syndrome) have increased abdominal VAT **as well as** increased abdominal SAT? I am raising this issue with regard to the potential off-label treatment of centrally obese HIV- people with Egrifta (assuming it is approved for use in HIV-associated lipodystrophy). In addition to the fact that the immunologic risk-benefit paradigm in HIV- centrally obese people treated with Egrifta is currently unknown and **may** not be as favourable as it appears to be in Egrifta-treated HIV+ centrally obese patients, treatment of centrally obese HIV- people with Egrifta with increased abdominal SAT **but without increased abdominal VAT** would not be very efficacious in that Egrifta does not substantially reduce abdominal SAT. In this regard, it is **highly unlikely** that physicians prescribing Egrifta off-label for centrally obese HIV- negative people will obtain a pre-treatment CT scan to quantitate the amount of abdominal VAT present.
6. Is there any consensus in the literature with regard to a cut-point (in cm²) which defines an increased level of abdominal VAT (as measured by CT scan)?

Please provide me with a succinct but thorough, point-by-point discussion of these questions (citing the most current references available). If you addressed some of these issues already in the NDA submission, please direct me to the proper location in your submission as well.

I am going to research some of these issues independently, but I would very much appreciate your response as soon as feasible.

Thank you,

RSP

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THE RATECHNOLOGIES INC	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

10/14/2009

Questions/information requests sent via email by Robert Perlstein to sponsor on October 5, 2009

TELECON

Date of Telecon	30 Sept 2009 1700 hours
Participants	Dr. Robert Perlstein (RP) (Medical Officer, Division of Metabolism and Endocrinology Drug Products/FDA) and Michelle Wilson (MW) (Kendle)
Telephone No	(301) 796-1270
Subject	Clarifications regarding 120-day Update Submission on 29Sept09
Prepared by	MW and then extensively edited by RP

RP was initially confused as to how to navigate the 120-day update. Once oriented to the contents of the 120-day update by MW, RP had the following questions, requests, and comments:

1. Where is the **full response** to point 1 in the Division's 74-day letter located in the 120-day update? As clearly indicated in the 74-day letter, the Division does indeed want the sponsor to perform the requested analyses (using Week 26 as baseline and Week 52 as study end), in addition to providing the supporting datasets for use by the Agency's statisticians.

2. Are the datasets submitted on 29 Sept09 for the pivotal Phase 3 studies, as well as the ISE/ISS, the same as those submitted on 29 May09 or not? Is that where the new datasets using Week 26 as baseline and Week 52 as study end requested in the 74-day letter are located?

3. Immunology

a. Please confirm that the 29Sept09 amended immunogenicity report contains all of the information in the 29May09 immunogenicity report, and that all new information is *italicized*.

b. RP would like Theratechnologies to walk him through the individual patient immunogenicity profiles referred to (and linked) in the cover letter for the 29Sept09 submission (sometime next week). How do these individual patient profiles integrate with the amended immunology report in Module 5?

c. Is the report in Module 5.3.1.4, E-PCL-250 Amendment 1 a totally new NAb validation report? If not, what has changed since the NAb validation report was submitted on 29May09? Please resubmit using *italics* to indicate what has changed.

d. Where in the 29Sept09 amended immunogenicity report is the data depicting follow-up antibody levels in IgG+ patients at Week 52 (in both pivotal studies) after Tesamorelin was permanently discontinued? How long were these patients followed? Were they followed until their antibody titers completely disappeared?

e. Approximately 50% of patients treated with Tesamorelin develop IgG binding antibodies to Tesamorelin at Week 26 (and Week 52 [the T-T group]). Is there information in the amended immunogenicity report which indicates how many patients manifest IgG binding antibodies to GRF after treatment with Tesamorelin at Week 26 (and Week 52 [the T-T group])? Do **all** patients who develop IgG binding antibodies to GRF after treatment with Tesamorelin at Week 26 (and Week 52 [the T-T group]) also manifest IgG binding antibodies to Tesamorelin, i.e. the patients who develop IgG binding antibodies to GRF are a subset of the cohort who develop IgG binding antibodies to Tesamorelin?

f. In the T-P group, please remind me what your rationale was for only measuring anti-GRF NAb (and not anti-Tesamorelin NAb as well) in the patients who were IgG binding antibody + at Week 52.

g. In the T-T group, you compared the IGF-1 response **only** (and not the VAT response) in the IgG+ anti-GRF NAb+ vs. the IgG+ anti-GRF NAb- vs. the IgG- anti-GRF NAb- groups at Week 52 (and also in the “T” group at Week 26). In contrast, in the T-T group, you compared **both** the IGF-1 response and the VAT response in the IgG+ anti-Tesamorelin NAb+ vs. the IgG+ anti-Tesamorelin NAb- vs. the IgG- anti-Tesamorelin NAb- groups at Week 52 (and also in the “T” group at Week 26). What was your rationale for this different approach?

4. What has changed in the following reports in the 29Sept09 submission (compared to the 29May09 submission)?

- 2.5 (Clinical Overview)
- 2.74 (Summary of Clinical Safety)
- ISS in Module 5

If there are changes, please resubmit these reports using *italics* to indicate what has changed.

5. What are the changes to the label in the 29Sept09 submission (compared to the label in the 29May09 submission)? Please reflect these changes in a MS word document using the tracking tool.

6. Studies in HIV- populations:

a. Please summarize thoroughly but succinctly the immunogenic response to Tesamorelin across all studies conducted in HIV- subjects, i.e. healthy normals, diabetics, sleep study, etc. Include the important baseline characteristics/demographics of these patients, the underlying disease, **the dose and duration of Tesamorelin treatment**, the number of IgG+ subjects and at what point they became IgG+. Please submit this information as an addendum to the recently submitted amended immunogenicity report. This information may give us some very preliminary insight into the immunogenic risk-benefit paradigm in HIV- patients. Given our mutual concern regarding the potential off-label use of Tesamorelin in HIV- obese subjects (if the drug is approved for use in patients with HIV lipodystrophy), this information has relevance.

b. Please indicate if there is any serum left for possible anti-GRF and/or anti-Tesamorelin NAb testing in these HIV- subjects.

c. As discussed in a recent telecon, based on unfortunate past experiences, the Division's immunology consultants believe that the apparently favourable, immunologic risk-benefit paradigm in relatively immunocompetent HIV+ patients with lipodystrophy treated with Tesamorelin does not necessarily mean that the immunologic risk-benefit paradigm would be as favourable if Tesamorelin (if approved) is prescribed off-label to large numbers of more immunocompetent HIV- obese patients. As we also discussed during that telecon, please submit what you consider to be an appropriate REMS (sooner rather than later) which would diminish the likelihood of substantial off-label use of Tesamorelin in the HIV- obese population. It is likely that this issue will be a significant topic of interest at the Advisory Committee Meeting projected for 2/24/10.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THE RATECHNOLOGIES INC	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

10/07/2009

Memorandum of telecon held between Robert Perlstein and sponsor on September 30, 2009 (clarification questions/requests regarding sponsor 120-day update submission on September 29, 2009)

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Friday, September 11, 2009 1:41 PM
To: 'wilson.michelle@kendle.com'
Subject: NDA 22-505: Egrifta PLR Format Comments
Attachments: Egrifta PLR Format Comments to Sponsor.doc

Dear Michelle,

We have done a preliminary PLR format review of the Egrifta label and have some comments for you. Please incorporate these revisions into the labeling and submit a revised package insert by Friday, October 9, 2009. We will use the revised package insert for further review of the label.

Please let me know if you have any questions.

Many thanks,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

PLR Format Review Comments
NDA 22-505 Egrifta (tesamorelin acetate) for Injection, 1 mg/vial

Please address the following identified deficiencies/issues and re-submit labeling by **October 9, 2009**. Your revised labeling will be used for further labeling discussions.

General

- Some discrepancies were noted between the Word and SPL versions of the package insert. Where these discrepancies exist, they are noted in the relevant sections below. Please be sure that the content contained in the Word version matches that of the content contained in the SPL version.

Highlights

Beginning of Highlights

- Remove the TM symbol after EGRIFTA. Do not use the TM symbol after the drug name in Highlights or the Table of Contents. Use the TM symbol only once in the content of labeling (FPI).

Dosage Forms and Strengths

- The proposed labeling states “1.1 mg” as the dosage strength to include the overfill amount of 0.1 mg. The proposed dosage strength is not acceptable because it should not include the overfill amount. Revise the dosage strength to state “1 mg”. In addition, clarify whether the dosage strength denotes the free base or the salt form of the peptide because the established name of the product should correlate with the dosage strength (1 mg tesamorelin or 1 mg tesamorelin acetate).
- Delete “55 mg mannitol” from this section. The listing of excipients should only appear in the Description section of the package insert.

Adverse Reactions

- Add the numerical reference to the appropriate corresponding section (Adverse Reactions) of the FPI to the end of the summarized statement.

Drug Interactions

- Add the numerical reference to the appropriate corresponding section(s) of the FPI to the end of the summarized statement.

End of Highlights

- Add the phrase “and Medication Guide” to the end of the statement “See Section 17 for PATIENT COUNSELING INFORMATION”. We note that this phrase was present in the SPL version of the package insert, but not in the Word version. The content contained in the SPL version must match that contained in the Word version.

Revision Date

- Add, in bold type, a revision date in the following format: “Revised: Month/Year” (i.e., Revised: August 2009 or Revised: 8/2009). We note that the revision date was present in the SPL version of the package insert, but not in the Word version. The content contained in the SPL version must match that contained in the Word version.

FPI: Contents

- Adjust the formatting of the two columns contained in the Table of Contents so that this section does not exceed ½ page.
- A horizontal line must be located between the Table of Contents and the FPI.
- There should be no periods after the numbers for the section or subsection headings. Remove the periods that follow the subsection numbers for these specific subsections: 2.1, 2.2, 5.1, 5.3, 5.4, 5.5, 6.1 and 6.2. This applies to the corresponding subsections in the FPI as well.

FPI

DOSAGE FORMS AND STRENGTHS

- The proposed labeling states “1.1 mg” as the dosage strength to include the overfill amount of 0.1 mg. The proposed dosage strength is not acceptable because it should not include the overfill amount. Revise the dosage strength to state “1 mg”. In addition, clarify whether the dosage strength denotes the free base or the salt form of the peptide because the established name of the product should correlate with the dosage strength (1 mg tesamorelin or 1 mg tesamorelin acetate).
- Delete “55 mg mannitol” from this section. The listing of excipients should only appear in the Description section of the package insert.

WARNINGS AND PRECAUTIONS

- Change the font from all capital letters to regular font in the subsection “5.4 Laboratory Tests” to match other subsections.

ADVERSE REACTIONS

- Bold type should not be used within subsections. Use another method to emphasize sub-sub-headings, such as italics or underline.

CLINICAL PHARMACOLOGY

- Bold type should not be used within subsections. Use another method to emphasize sub-sub-headings, such as italics or underline.

HOW SUPPLIED/STORAGE AND HANDLING

- The proposed labeling states “1.1 mg” as the dosage strength to include the overfill amount of 0.1 mg. The proposed dosage strength is not acceptable because it should not include the overfill amount. Revise the dosage strength to state “1 mg”. In addition, clarify whether the dosage strength denotes the free base or the salt form of the peptide because the established name of the product should correlate with the dosage strength (1 mg tesamorelin or 1 mg tesamorelin acetate).
- Delete “55 mg mannitol” from this section. The listing of excipients should only appear in the Description section of the package insert.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22505	ORIG-1	THERATECHNOLOGIES, INC.	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON

09/11/2009

Email sent to sponsor on 9/11/09, requesting revisions to PLR label



NDA 22-505

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Theratechnologies Inc.
c/o Kendle International Inc.
441 Vine Street, Suite 500
Cincinnati, Ohio 45202

ATTENTION: Michelle Wilson, Ph.D.
Senior Regulatory Consultant, Kendle International, Inc.

Dear Dr. Wilson:

Please refer to your New Drug Application (NDA) dated May 29, 2009, received May 29, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tesamorelin Acetate for Injection, 1.1 mg per vial.

We also refer to your June 17, 2009, correspondence, received June 17, 2009 requesting review of your proposed proprietary name, Egrifta. We have completed our review of the proposed proprietary name, Egrifta, and have concluded that it is acceptable.

The proposed proprietary name, Egrifta, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your June 17, 2009, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Millie Wright, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-1027. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Jennifer Johnson at (301) 796-2194.

Sincerely,
{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
----- NDA 22505	----- ORIG 1	----- NO FIRM	----- TESAMORELIN ACETATE

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/s/

DENISE P TOYER on behalf of CAROL A HOLQUIST
08/26/2009

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): CDER OSE CONSULTS Division of Risk Management (DRISK) Attn: Mildred Wright, Project Manager WO22, Room 4492, (301) 796-1027		FROM: Jennifer Johnson, Regulatory Project Manager Division of Metabolism and Endocrinology Products, HFD-510 WO22, Room 3114, (301) 796-2194 jennifer.johnson@fda.hhs.gov		
DATE August 25, 2009	IND NO. N/A	NDA NO. 22-505	TYPE OF DOCUMENT Original NDA	DATE OF DOCUMENT May 29, 2009
NAME OF DRUG Egrifta (tesamorelin acetate) for Injection, 1 mg/vial		PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG GnRH analog	DESIRED COMPLETION DATE January 22, 2010
NAME OF FIRM: Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Please review the patient labeling (Instructions for Use) and Medication Guide submitted with this NDA, a new molecular entity. The NDA was submitted on May 29, 2009. The patient Instructions for Use and Medication Guide are located at the end of the package insert (SPL version) of the original NDA submission dated May 29, 2009; however, per my request the applicant submitted on July 31, 2009 the Word versions of the patient Instructions for Use and Medication Guide. (This NDA is all-electronic, and the July 31 st submission can be accessed via the following EDR link: \ICDSESUB1\EVSPROD\NDA022505\0005 .) The clinical reviewer is Robert Perlestein and the DMEPA reviewer is Cathy Miller. The PDUFA goal date is March 29, 2010. Please feel free to contact me with any questions or concerns. Many thanks, Jennifer (6-2194)				
SIGNATURE OF REQUESTER Jennifer Johnson		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DARRTS <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
-----	-----	-----	-----
NDA 22505	ORIG 1	NO FIRM	TESAMORELIN ACETATE
NDA 22505	ORIG 1	NO FIRM	TESAMORELIN ACETATE

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/s/

JENNIFER L JOHNSON
08/25/2009



NDA 22-505

FILING COMMUNICATION

Kendle International Inc.
Attention: Michelle Wilson, Ph.D.
Senior Regulatory Consultant
U.S. Agent for Theratechnologies Inc.
441 Vine Street, Suite 500
Cincinnati, OH 45202

Dear Dr. Wilson:

Please refer to your new drug application (NDA) dated May 29, 2009, received May 29, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Egrifta (tesamorelin acetate) for Injection, 1 mg/vial.

We also refer to your submissions dated June 17, 25, and 30, 2009.

We have completed our filing review and have determined that your supplemental application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this supplemental application is considered filed 60 days after the date we received your supplemental application. The review classification for this supplemental application is **Standard**. Therefore, the user fee goal date is **March 29, 2010**.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by February 8, 2010.

During our filing review of your application, we identified the following potential review issues and have the following requests for additional information:

Clinical/Biostatistics

1. Provide Week 26 through 52 analyses using re-randomization at Week 26 as baseline, and the efficacy (VAT, trunk fat, total fat, abdominal SAT, limb fat, etc) datasets for

Studies TH9507-CTR-1012 and LIPO/010 EXT. More specifically, provide additional “vertical data” which uses multiple flag variables to subset the population, e.g., intent-to-treat (ITT), completers, observed cases, last observation carried forward (LOCF), etc. The datasets submitted should include the investigator’s name (e.g., initials, not only the investigator number). The names should be consistent between the two studies for those investigators who participated in both studies.

2. Please provide as soon as possible neutralizing antibody (NAb) results at Week 26, and comparisons of the IgG+ NAb+ groups versus (a) the IgG+ NAb- groups and (b) the IgG- groups, with regard to increase in serum IGF-1 and decrease in VAT for each pivotal study and for both studies pooled.

Chemistry, Manufacturing and Controls

3. The proposed labeling states “1.1 mg” as the dosage strength to include the overfill amount of 0.1 mg. The proposed dosage strength is not acceptable because it should not include the overfill amount. Revise the dosage strength to state “1 mg”. In addition, clarify whether the dosage strength denotes the free base or the salt form of the peptide because the established name of the product should correlate with the dosage strength (i.e., 1 mg tesamorelin or 1 mg tesamorelin acetate).

Microbiology

4. Provide a justification for why dosing is proposed with two vials containing 1 mg of product each rather than a single vial containing 2 mg of product.

Safety/Medication Error and Prevention

5. Provide a mock kit of the product (to include both drug and sterile water, as well as all syringes and needles included in the package).

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the

product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult the Division of Metabolism and Endocrinology Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

(b) (4)

Once we have reviewed your request, we will notify you if the partial waiver request is denied. For the pediatric studies you wish to defer, please submit a pediatric development plan within 30 days of the date of this letter. A pediatric drug development plan must address the indication proposed in this application.

If you have any questions, call Jennifer Johnson, Regulatory Project Manager, at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

ERIC C COLMAN

08/10/2009

Eric Colman for Mary Parks

REQUEST FOR STUDY ENDPOINTS CONSULTATION

TO (Division/Office): Study Endpoints and Label Development Team (SEALD) CDER/OND-IO White Oak Bldg 22, Mail Drop 6411			FROM (Division/Office): Jennifer Johnson, Regulatory Project Manager, WO22 Room 3114, 6-2194 and Robert Perlstein, Clinical Reviewer, WO22 Room 3370, 6-1270 Division of Metabolism and Endocrinology Products, HFD-510	
DATE OF CONSULT REQUEST July 13, 2009	IND/NDA/BLA NO. NDA 22-505	SERIAL NO/SUPPL. NO.	TYPE OF DOCUMENT New NDA (NME)	DATE OF DOCUMENT May 29, 2009
NAME OF DRUG Egrifta (tesamorelin acetate) for Injection		NAME OF SPONSOR/APPLICANT Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)		CLASSIFICATION OF DRUG GHRH analog
			REQUESTED COMPLETION DATE September 14, 2009	

DRUG DEVELOPMENT PHASE (pre-IND/NDA/BLA; IND/BB-IND Phase I, II, III; NDA/BLA): NDA

PDUFA date (if associated with NDA/BLA): March 29, 2010

MEETING DATES FOR SUBMISSION (IF APPLICABLE) N/A

Internal: _____ Sponsor: _____

MEETING TYPE (A, B, C):

STUDY ENDPOINT REVIEW (PLEASE FILL IN THE APPROPRIATE INFORMATION)

PROPOSED INDICATION (edited by the Division's clinical reviewer): To induce and maintain a reduction of excess abdominal visceral adipose tissue (VAT) in HIV-infected AIDS patients with HIV-associated adipose redistribution syndrome (HARS).

INSTRUMENT(S) TO BE EVALUATED: See below

IS A COPY OF INSTRUMENT(S) TO BE REVIEWED INCLUDED IN THE SUBMISSION? YES

IF NOT, PLEASE OBTAIN A COPY FROM THE SPONSOR/APPLICANT

CONSULT REVIEW REQUESTED (PLEASE FILL IN A BRIEF SUMMARY OF WHAT IS BEING REQUESTED; INCLUDE INFORMATION ON THE TYPE OF DOCUMENT BEING REVIEWED SUCH AS SPA, PEDIATRIC WR, PROTOCOL)

A. PRO consult regarding the NME, Tesamorelin (a novel GHRH analog), developed to reduce abdominal visceral adipose tissue (VAT) in HIV+ AIDS patients with HARS:

1. Please review the **separate PRO Report** in Section 5.3.5.3.1 of the NDA, as well as the PRO information contained in the:

- 1) Summary of Clinical Efficacy (Section 2.7.3);
- 2) Clinical Study Report LIPO 010 (Section 5.3.5.1) (the first Phase III pivotal study);
- 3) Clinical Study Reports CTR 1011 and 1012 (Section 5.3.5.1) (the second Phase III pivotal study); and
- 4) **Package Insert (Section 1.14.1.2) (last paragraph of Section 14 of the PI).**

For your convenience, here is the direct link to the EDR submission: <\\CDSESUB1\EVSPROD\NDA022505\0000>

B. Specific Questions:

1. As you requested at the pre-NDA meeting held on September 19, 2008, Ralph Turner's Phase V validation materials have apparently been included in the May 29, 2009 NDA submission. **Are these validation materials sufficient for SEALD purposes?** (Please note that Jane Scott and Laurie Burke approved similar Phase V validation materials once before several years ago when submitted by Serono.)

2. As conveyed to Laurie Burke and Paivi Miskala via email in September 2008, Laurie Burke **explicitly** indicated (to the clinical reviewer, Dr. Robert Perlstein, in 2007 during the review of Serono's submission) that the use of the baseline-established, minimally beneficial change in BPA **as well as** the change score for BPA post-treatment in the calculation of the responder criteria for BAD and BSE, makes the use of the change score for BPA **off-limits as a usable/reportable endpoint**

(in particular, in the PI). Please clarify this specific question.

3. As was the case with Serono's Serostim submission for the same indication in 2006-2007, the responder criteria for BAD and BSE round off to **2 scale units** (25 points for BAD and 50 points for BSE). Please recall the teleconference that took place between Dr. Perlstein, Laurie Burke, and Ralph Turner in Laurie's office in the spring of 2007. At that time, Laurie was **very pleased** with the more rigorous 2 scale unit (as opposed to 1 scale unit) responder criteria for BAD and BSE. **Do you still feel the same way?**

Note: This clinical reviewer is very familiar with the statistical analyses that the sponsor has performed on BAD, BSE and BPA (between-group ANCOVA for the change scores, Fisher's exact test for the between-group comparison of the number of responders, etc), and will consult with our statisticians as necessary.

Please feel free to contact us with any questions or concerns. Paivi Miskala and Laurie Burke were the SEALD consultants at the pre-NDA meeting conducted in the fall of 2008. Please convey this consultation to them.

Many thanks,

Rob Perlstein and Jennifer Johnson

SIGNATURE OF REQUESTER Jennifer Johnson	METHOD OF DELIVERY (Check one) <input type="checkbox"/> INTEROFFICE MAIL <input type="checkbox"/> HAND -CARRIED <input checked="" type="checkbox"/> E-MAIL/DFS
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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this page is the manifestation of the electronic signature.**

/s/

Jennifer Johnson
7/13/2009 11:25:29 AM

REQUEST FOR CONSULTATION

TO (Division/Office): **Susan Kirshner, Ph.D. and Daniela Verthelyi, Ph.D.**
Office of Pharmaceutical Science
Office of Biotechnology Products, Division of Therapeutic Proteins

FROM: **Jennifer Johnson, Regulatory Project Manager**
Division of Metabolism and Endocrinology Products, HFD-510
WO22 Room 3114, (301) 796-2194
jennifer.johnson@fda.hhs.gov

DATE
July 10, 2009

IND NO.
61,226

NDA NO.
22-505

TYPE OF DOCUMENT
New NDA (NME)

DATE OF DOCUMENT
May 29, 2009 and June 29, 2009

NAME OF DRUG
Egrifta (tesamorelin acetate) for Injection

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG
GHRH analog

DESIRED COMPLETION DATE
October 1, 2009

NAME OF FIRM: **Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)**

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE--NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | | |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- | | |
|--|---|
| <input type="checkbox"/> TYPE A OR B NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|---|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG EXPERIENCE

- | | |
|--|--|
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

A. Immunology consult regarding the NME, Tesamorelin (a novel GHRH analog), developed to reduce abdominal visceral adipose tissue (VAT) in HIV+ AIDS patients with HIV-associated adipose redistribution syndrome (HARS):

1. Please refer to Amendment 3 to NDA 22-505 submitted on June 29, 2009, which contains the sponsor's answers to your 3 requests for clarification regarding the NAb assay, as stated in our letter issued to the sponsor under IND 61,226 on June 22, 2009. For your convenience, this letter, as well as the cover letter of the June 29, 2009 submission, are attached to this consult request. Additionally, here is the direct link to this EDR submission:

<http://CDSESUB1NEVSPRODINDA0225050003>

Please convey to the Division as rapidly as possible that you are now hopefully completely satisfied with the validity/qualification of this assay.

2. Please review the separate **Immunogenicity Report** in Section 5.3.5.3.1 of the NDA, as well as the immunology information contained in the:

- 1) Summary of Clinical Safety (Section 2.7.4);
- 2) Clinical Study Report LIPO 010 (Section 5.3.5.1) (the first Phase III pivotal study);
- 3) Clinical Study Reports CTR 1011 and 1012 (Section 5.3.5.1) (the second Phase III pivotal study); and
- 4) **Package Insert** (Section 1.14.1.2) (last paragraph of Section 6.2 of the PI regarding IgG+ NAb+ patients and Section 5.1/5.3 of the PI regarding hypersensitivity/injection site reactions).

B. Specific Questions:

1. Do you agree that the comparable efficacy (decrease in VAT and increase in serum IGF-1) observed in:

- 1) IgG+ and IgG- patients at Week 26 and Week 52;
 - 2) **IgG+ NAb+**, IgG+ NAb-, IgG- NAb- patients treated with Tesamorelin for 52 weeks (the T-T groups); and
 - 3) **IgG+ NAb+**, IgG+ NAb-, IgG- NAb- patients treated with Tesamorelin for 26 weeks followed by Placebo for 26 weeks (the T-P groups)
- indicates that the in vitro finding of Tesamorelin and native GRF NABs in ~10% and ~5%, respectively, of Tesamorelin-treated patients at Week 52 **is not clinically consequential?** (Note: The sponsor has promised to provide the Division with additional NAB data for patients treated with Tesamorelin for 26 weeks within several months.)

2. Do you agree that all patients who are **IgG+ plus/minus NAb+** at Week 52 should be followed indefinitely (on or off Tesamorelin) with respect to antibody titers, and periodic measurements of VAT and serum IGF-1?

3. If Tesamorelin is approved for the requested indication (increased abdominal VAT in HIV+ AIDS patients with HARS), the Division is concerned about the off label use of Tesamorelin in the huge number of **immunocompetent**, obese HIV- people in the USA (who clearly all have excessive amounts of abdominal subcutaneous adipose tissue (SAT) **plus/minus** increased abdominal VAT). More specifically, we are concerned that the immunologic risk-benefit paradigm would be different/possibly more risky in the **immunocompetent**, centrally obese HIV- target population. As a consequence, the Division is seriously considering a mandatory requirement for restricted distribution if this drug is approved for HIV+ AIDS patients with HARS and increased abdominal VAT. **Please give us your clinical immunology perspective on this very important matter**. Note: More than likely, this NDA will be discussed at an Advisory Committee (AC), and we may possibly request your participation at the AC with regard to the issue described above in paragraph B.3.

Susan: Please call Dr. Perlstein at your very earliest convenience (703-909-0045) after you receive this consult (ideally on July 13 or 14, 2009 before the filing meeting on July 15, 2009).

Many thanks,
Jennifer

SIGNATURE OF REQUESTER
Jennifer Johnson

METHOD OF DELIVERY (Check one)
 DFS/EMAIL HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER



IND 61,226

Kendle International, Inc.
US Agent for Theratechnologies, Inc.
Attention: Michelle Wilson, Ph.D.
Senior Regulatory Consultant
1200 Carew Tower, 441 Vine Street
Cincinnati, OH 45202

Dear Dr. Wilson:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for TH9507 (tesamorelin) for injection.

We also refer to your amendment dated February 26, 2009, containing information on the proposed neutralizing assay, submitted in response to our letter dated February 20, 2009.

We have the following comments and requests for additional information. Please note that these requests are not clinical hold issues. However, response to them is requested:

1. Provide data supporting the selection of (b) (4) nM Tesmorelin or rGRF as the stimulatory dose. The Agency recommends that the stimulatory dose selected should be between 40 – 70% of the maximum response of the linear portion of the dose-response curve for the cells. Alternative choices may be appropriate but should be supported by a strong scientific rationale and appropriate data.
2. With regard to the NAb assay negative cut-off determinations (for “potentially positive results”), provide the data and formulas used for your determination of the cut-off values (either the NCO factors or the serum source correction factors).
3. Provide the expected concentration of cAMP in stimulated BHK-C5-G1 cells.

If you have any questions, contact Kati Johnson, Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Linked Applications

Sponsor Name

Drug Name / Subject

IND 61226

THERATECHNOLOGIES
INC

TH9507 FOR INJECTION

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/s/

MARY H PARKS

06/22/2009

25-June-2009

Mary Parks, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products
Attention: Document Room
5901-B Ammendale Road
Beltsville, MD 20705

Subject: **EGRIFTA™ (tesamorelin acetate for injection)**
NDA 22-505
Serial No: 0003
Amendment to a Pending Application: Response to FDA request for information regarding Nab Method; Revised 1.6.3.

Dear Dr. Parks,

Reference is made to the Theratechnologies' New Drug Application 22-505 for EGRIFTA™ (tesamorelin acetate for injection) which is intended to be indicated to induce and maintain a reduction of excess abdominal fat in HIV-infected patients with lipodystrophy. Kendle International has been designated the US agent for this IND.

Included within the body of this cover letter is Theratechnologies' response to the information requested in the Agency letter dated 22 June 2009 regarding Theratechnologies' Neutralizing Antibody (Nab) method following review of package provided under serial number 143 of IND #61,226.

1. Provide data supporting the selection of (b) (4) nM Tesamorelin or rGRF as the stimulatory dose.

The Agency recommends that the stimulatory dose selected should be between 40 – 70% of the maximum response of the linear portion of the dose-response curve for the cells. Alternative choices may be appropriate but should be supported by a strong scientific rationale and appropriate data.

Response

The data supporting the selection of (b) (4) nM for the stimulatory dose of tesamorelin or hGRF concentrations for the neutralization assays can be found in the method development reports E-PCL-238 and E-PCL-239 (Figure 1 of both reports) filed in section 5.3.1.4 of this NDA. The selected stimulatory doses were targeted to be approximately (b) of the maximum dose. Note that, due to the variability of the tesamorelin or hGRF dose response curves, the % of the maximal dose will vary from day to day; however, assay performance is not

affected, as a positive control is always included and the response has to be below the negative control.

2. With regard to the NAb assay negative cut-off determinations (for “potentially positive results”), provide the data and formulas used for your determination of the cut-off values (either the NCO factors or the serum source correction factors).

Response

The data for the cut-off values are presented in statistical reports in [Appendix 8](#) of the neutralization assay method validation (E-PCL-248 filed in section 5.3.1.4 of this NDA).

(b) (4)



(b) (4)



Table 1 Softmax pro layout of NC results for NCO estimates



(b) (4)

(b) (4)



(b) (4)



Also included in this amendment is a revised [1.6.3](#) Correspondence regarding meetings.

All electronic files included in this submission are approximately 5 Mb. All files were checked and verified to be free of viruses, prior to being transmitted using Symantec Antivirus Corporate Edition, program version 8.1.0.825 and scan engine version 4.2.0.7 with a virus definition date of 24 June 2009, revision 3. The IT point of contact for this



submission is

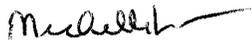
(b) (4)

(b) (4)

The confidentiality of this submission, and all information contained herein, is claimed by Theratechnologies under all applicable laws and regulations. Disclosure of any such information is not authorized without prior written authorization from Theratechnologies.

Should you have any comments regarding this submission, please contact Dr. Wilson at (513) 258-5766.

Sincerely,



Michelle Wilson, Ph.D.
Senior Regulatory Consultant
Kendle International Inc.

cc: Martine Ortega; Vice President, Compliance and Regulatory Affairs;
Theratechnologies Inc.
Nadine Bouchard; Director, Compliance/Associate, Regulatory Affairs;
Theratechnologies Inc.

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/s/

Jennifer Johnson
7/13/2009 11:04:16 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): CDER/OPS Jim McVey james.mcvey@fda.hhs.gov Microbiologist New Drug Microbiology WO51 Room 4162 Phone: 301-796-5723		FROM: Jennifer Johnson Regulatory Project Manager jennifer.johnson@fda.hhs.gov DMEP, HFD-510 WO22 Room 3114 Phone: 301-796-2194		
DATE June 25, 2009	IND NO. 61,226	NDA NO. 22-505	TYPE OF DOCUMENT Original NDA	DATE OF DOCUMENT May 29, 2009
NAME OF DRUG Egrifta (tesamorelin acetate) for Injection, 1.1 mg/vial	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG GnRH analog	DESIRED COMPLETION DATE January 22, 2010	
NAME OF FIRM: Theratechnologies Inc. (U.S. Agent: Kendle International Inc.)				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (<i>SPECIFY BELOW</i>):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Please review this NDA for sterility assurance. This document can be found in the EDR (see link below). The related IND is 61,226. Please note that this drug is a new molecular entity (NME). The CMC reviewers are Su Tran (initial quality assessment) and Joseph Leginus. Direct link to EDR: \CDSESUB\1\EVSPROD\NDA022505\0000 Feel free to contact me with any questions or concerns. Many thanks, Jennifer				
SIGNATURE OF REQUESTER Jennifer Johnson		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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this page is the manifestation of the electronic signature.**

/s/

Jennifer Johnson
6/25/2009 04:17:15 PM



NDA 22-505

NDA ACKNOWLEDGMENT

Kendle International Inc.
Attention: Michelle Wilson, Ph.D.
Senior Regulatory Consultant
U.S. Agent for Theratechnologies Inc.
441 Vine Street, Suite 500
Cincinnati, OH 45202

Dear Dr. Wilson:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Egrifta (tesamorelin acetate) for Injection

Date of Application: May 29, 2009

Date of Receipt: May 29, 2009

Our Reference Number: NDA 22-505

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on **July 28, 2009** in accordance with 21 CFR 314.101(a).

Please note that you are responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) (42 USC §§ 282(i) and (j)), which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) control numbers. 42 USC 282(j)(5)(B). You did not include such certification when you submitted this application. You may use Form FDA 3674, *Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank*, to comply with the

certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trials referenced in this application. Additional information regarding the certification form is available at: http://internet-dev.fda.gov/cder/regulatory/FDAAA_certification.htm. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information on registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrinology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call me at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Jennifer Johnson
6/17/2009 11:42:17 AM