HORIZON PHARMA PLC

FORM 10-K/A
(Amended Annual Report)

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K/A
(Amendment No. 3)

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2014

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____to _____

Commission File Number 001-35238

HORIZON PHARMA PUBLIC LIMITED COMPANY
(Exact name of Registrant as specified in its charter)

Ireland	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
Connaught House, 1 st Floor 1 Burlington Road, Dublin 4, D04 C5Y6, Ireland	**Not Applicable**
(Address of principal executive offices)	**(zip code)**

011 353 1 772 2100
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Ordinary shares, nominal value $0.0001 per share	**The NASDAQ Global Select Market**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐.

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒.

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined by Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's voting ordinary shares held by non-affiliates of the registrant, based upon the $15.82 per share closing sale price of the registrant's ordinary shares on June 30, 2014 (the last business day of the registrant's most recently completed second quarter), was approximately $1.0 billion. Solely for purposes of this calculation, the registrant's directors and executive officers and holders of 10% or more of the registrant's outstanding ordinary shares have been assumed to be affiliates and an aggregate of 9,164,811 shares of the registrant's voting ordinary shares held by such persons on June 30, 2014 are not included in this calculation.

As of February 20, 2015, the registrant had outstanding 125,100,210 ordinary shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the registrant's 2015 Annual Meeting of Shareholders are incorporated by reference into Part III of the registrant's Annual Report on Form 10-K.

EXPLANATORY NOTE

Horizon Pharma Public Limited Company (the "Company") is filing this Amendment No. 3 to Annual Report on Form 10-K/A (this "Amendment") to amend the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2014, as filed with the Securities and Exchange Commission (the "SEC") on February 27, 2015 and as previously amended on March 2, 2015 and April 10, 2015 (the "10-K"). This Amendment is being filed solely to re-file revised redacted versions of Exhibits 10.62 and 10.65 to the 10-K, reflecting changes to the Company's confidential treatment request with respect to certain portions of such exhibits. In addition, as required by Rule 12b-15 under the Securities Exchange Act of 1934, as amended, new certifications by the Company's principal executive officer and principal financial officer are filed as exhibits to this Amendment.

No attempt has been made in this Amendment to modify or update the other disclosures presented in the 10-K. This Amendment does not reflect events occurring after the filing of the 10-K or modify or update those disclosures that may be affected by subsequent events. Accordingly, this Amendment should be read in conjunction with the 10-K and the registrant's other filings with the SEC.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this Annual Report on Form 10-K/A to be signed on its behalf by the undersigned, thereunto duly authorized.

Horizon Pharma plc

By: /s/ Paul W. Hoelscher
Paul W. Hoelscher

Executive Vice President and
Chief Financial Officer
(Principal Financial Officer)

Dated: May 26, 2017

INDEX TO EXHIBITS

Exhibit Number	Description of Document
10.62**	License Agreement for Interferon Gamma, dated May 5, 1998, by and between Genentech, Inc. and Connetics Corporation.
10.65**	Amendment No. 3 to License Agreement for Interferon Gamma, dated April 27, 1999, by and between Genentech, Inc. and Connetics Corporation.
31.3	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.
31.4	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.

** Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

Exhibit 10.62

*****Text Omitted and Filed Separately
with the Securities and Exchange Commission.
Confidential Treatment Requested
Under 17 C.F.R. Sections 200.80(b)(4)
and 240.24b-2.**

LICENSE AGREEMENT FOR

INTERFERON GAMMA

This Agreement is entered into effective as of May 5, 1998, ("Effective Date") by and between Connetics Corporation, a Delaware corporation with its principal office at 3400 West Bayshore Road, Palo Alto, California 94303 ("Connetics"), and Genentech, Inc., a Delaware corporation with its principal office at 1 DNA Way, South San Francisco, California 94080 ("Genentech").

WHEREAS, Connetics wishes to obtain a non-exclusive license to manufacture and an exclusive license to use, sell, offer for sale and import Interferon Gamma (as defined herein) in the United States for the treatment of certain medical disorders;

WHEREAS, in consideration for the foregoing, Connetics will issue to Genentech shares of Connetics Common Stock on the terms and conditions set forth in that certain stock purchase agreement between Genentech and Connetics of even date herewith (the "Stock Agreement");

WHEREAS, Genentech will manufacture and supply Connetics with Interferon Gamma-1B (as defined herein) under the terms and conditions set forth in that certain supply agreement between Genentech and Connetics of even date herewith (the "Supply Agreement");

WHEREAS, Connetics and Genentech are parties to that certain Agreement on Interferon Gamma-1B dated December 8, 1995 (the "Prior Agreement") and desire to terminate the Prior Agreement effective as of the date hereof and to accept the rights and

obligations created pursuant hereto in lieu of the rights and obligations under the Prior Agreement; and

WHEREAS, Genentech and Connetics therefore agree to undertake the foregoing, all under the terms and conditions set forth in this Agreement and for the consideration set forth herein and in the Stock Agreement.

NOW, THEREFORE, in consideration of the mutual promises contained herein, the Parties agree as follows:

1.0 Definitions

1.1 "Best Efforts" shall mean every necessary and prudent effort of a Party applied in a prompt, commercially reasonable manner, to the maximum extent reasonably allowed by such Party's available financial resources, taking into account all of such Party's business commitments for such financial resources.

1.2 "Biogen License" shall mean that certain license agreement between Genentech and Biogen, Inc. ("Biogen") dated January 5, 1990, as amended on November 23, 1992.

1.3 "Biogen License Rights" shall mean all sublicenseable rights granted to Genentech by Biogen under the Biogen License.

1.4 "BLA" shall mean Biologics License Application.

1.5 "Bulk Product" shall mean Interferon Gamma-1B provided as bulk protein manufactured in compliance with Good Manufacturing Practices, pursuant to applicable FDA regulatory approvals and supplied to Connetics in such a form and in such containers as shall be mutually determined by Genentech and Connetics and as described in the Supply Agreement.

1.6 "C.F.R." shall mean Code of Federal Regulations.

1.7 "CGD" shall mean chronic granulomatous disease.

1.8 "Connetics Knowhow" shall mean all proprietary information, methods, processes, techniques and data that have not been publicly disclosed, that relate to Interferon Gamma and that arise out of Connetics' and its sublicensees' efforts in the development of Interferon Gamma (including Interferon Gamma as part of a Licensed Product) hereunder and that on the Effective Date and hereafter during the term of this Agreement are owned or controlled by Connetics or its sublicensees or under which Connetics or its sublicensees otherwise has the right to grant licenses or sublicenses.

1.9 "Connetics Patent Rights" shall mean all patents, patent applications and any patents issuing therefrom, together with any substitutions, extensions, reexaminations, reissues, renewals, divisions, continuations and continuations-in-part thereof, that (a) claim inventions constituting Interferon Gamma or its manufacture or use that arise out of Connetics' or its sublicensee's efforts in the development of Interferon Gamma (including Interferon Gamma as part of a Licensed Product) hereunder during the term of this Agreement, and (b) are owned by Connetics or its sublicensees or under which Connetics or its sublicensees otherwise has the right to grant licenses or sublicenses as provided herein.

1.10 "ELA" shall mean Establishment License Application.

1.11 "FDA" shall mean the United States Food and Drug Administration.

1.12 "Field of Use" shall mean the administration to humans of Licensed Product for the treatment or prevention of: (a) any dermatological disease or condition including, without limitation, atopic dermatitis, keloids/hypertrophic scars, pustular psoriasis and scleroderma, but excluding any cancer disease or condition, (b) any infectious disease or

condition including, without limitation, fungal, viral and bacterial infections, (c) osteopetrosis, (d) chronic granulomatous disease, (e) pulmonary fibrosis, and (f) asthma. Notwithstanding the foregoing, the Field of Use shall not include the administration to humans of Licensed Product for the treatment or prevention of any type of arthritis or cardiac or cardiovascular disease or condition, or use of Licensed Product for any indication or use in the field of oncology or endocrinology. Each of Subsections 1.12 (a) through (f) inclusive shall hereinafter each be referred to individually as an "Area of the Field of Use" and together as the "Areas of the Field of Use."

1.13 "Finished Product" shall mean Interferon Gamma-1B supplied in vialed form as 100 micrograms of Interferon Gamma-1B protein in a 0.5 ml fill volume and as described in the Supply Agreement, manufactured in compliance with Good Manufacturing Practices and intended for commercial sale to treat CGD and osteopetrosis and for clinical studies.

1.14 "Fully Burdened Non-human Interferon Gamma Manufacturing Cost" shall mean the cost of Genentech's production and testing of Non-human Interferon Gamma, which shall be comprised of the sum of: […***…].

1.15 "Gene Therapy" shall mean the therapeutic or prophylactic treatment of a human being with: (a) one or more oligonucleotides or nucleotide sequences, in native form

or chemically modified, which are introduced into the body in free form, bound to a carrier molecule, contained in any molecular vesicle (e.g. a liposome), incorporated into or attached to a vector of any type, contained in any cellular construct and/or contained in any mechanical device or (b) cells which have been manipulated ex vivo using one or more oligonucleotides or nucleotide sequences.

1.16 "Genentech Knowhow" shall mean all proprietary information, methods, processes, techniques and data that are in the possession or control of Genentech on the Effective Date or thereafter during the term of this Agreement, that Genentech is free to license or sublicense, that have not been publicly disclosed, and that are specific and reasonably necessary for the use, sale, offer for sale or importation of Interferon Gamma in the Field of Use in the Territory, but shall not include information regarding the manufacture of Interferon Gamma.

1.17 "Genentech Manufacturing Knowhow" shall mean all proprietary information, methods, processes, techniques and data that are in the possession of Genentech at such time as Genentech determines or is required pursuant to the terms of the Supply Agreement to make a manufacturing technology transfer to Connetics, that are not generally known, and that are specific and reasonably necessary for the manufacture of Interferon Gamma in the Field of Use in the Territory.

1.18 "Genentech Patent Rights" shall mean all patents and patent applications and any patents issuing therefrom, together with any extensions, reissues, reexaminations, substitutions, renewals, divisions, continuations and continuations-in-part thereof (a) that are owned or controlled by Genentech presently or hereafter, during the term of this Agreement, and under which Genentech is free to license or sublicense, and (b) to the extent they claim

or directly relate to Interferon Gamma or its manufacture or use in the Field of Use, including, without limitation, the patent rights granted under that certain license agreement between Genentech and […***…], dated July 16, 1990 (the "[…***…] License"), but specifically excluding any rights granted to Genentech under the Biogen License. Genentech Patent Rights shall include, without limitation, the patents and patent applications listed in Exhibit A attached hereto. Notwithstanding the foregoing, Genentech Patent Rights shall exclude any rights Genentech acquires after the Effective Date of this Agreement under third-party license agreements, with the exception of those acquired under the […***…] License, unless and until the Parties mutually agree on terms and conditions for the sublicense of such rights from Genentech to Connetics.

1.19 "IND" shall mean Investigational New Drug Application.

1.20 "Interferon Gamma" shall mean a polypeptide having the 126 amino acid sequence set forth on Exhibit B or a variant of such sequence having at least 70% homology thereto, or such polypeptide with one or more additional amino acid residue(s) extending from the N-terminus thereof and/or one or more additional amino acid residue(s) extending from the C-terminus thereof, such polypeptides including, without limitation, Interferon Gamma-1B.

1.21 "Interferon Gamma-1B" shall mean a single chain polypeptide containing the 140 amino acid sequence set forth on Exhibit C hereto, i.e., the active ingredient in the ACTIMMUNE ® (Interferon Gamma-1B) Injection product.

1.22 "Licensed Product" shall mean any pharmaceutical formulation containing Interferon Gamma whether alone or together with or incorporated into any other substance or product or material or device, whether active or not, and which (i) but for the licenses

granted hereunder, the manufacture, use, sale, offer for sale or importation of which in the Territory would infringe or contribute to the infringement of Genentech Patent Rights in the Territory, or (ii) is based upon or incorporates or utilizes Genentech Knowhow. For purposes of clarification, it is understood that this definition shall not include any pharmaceutical formulation which induces the presence or activity of Interferon Gamma *in vivo* , or the DNA encoding Interferon Gamma for Gene Therapy, or other biological techniques aimed at establishing or modulating endogenous Interferon Gamma in vivo.

1.23 "NDA" shall mean New Drug Application.

1.24 "NDC" shall mean National Drug Code.

1.25 "Net Sales" shall mean, as to each calendar quarter, the gross invoiced sales prices charged for all Licensed Products sold by Connetics and its sublicensees in arm's length transactions to independent third parties during such quarter, after deduction of the following items paid by Connetics and its sublicensees during such calendar quarter with respect to sales of Licensed Products regardless of the calendar quarter in which such sales were made, provided and to the extent that such items are incurred or allowed and do not exceed reasonable and customary amounts in the market in which such sales occurred:

(i) […***…];

(ii) […***…];

(iii) […***…]

[…***…]; and

(iv) […***…].

Notwithstanding the foregoing, no deduction shall be made for bad debt expense.

1.26 "Party" shall mean Genentech or Connetics, and, when used in the plural, shall mean both of them.

1.27 "PLA" shall mean Product License Application.

1.28 "Territory" shall mean the United States of America and its territories and possessions.

1.29 "Transfer Date" shall mean, unless otherwise mutually agreed to by the Parties, the last day of the second full calendar month following the first delivery by Connetics to Genentech of Connetics' labeling and packaging materials for Genentech's use in labeling and packaging Finished Product, pursuant to a purchase order submitted by Connetics and accepted by Genentech, to be sold commercially by Connetics for treatment of CGD, provided that the activities set forth on Exhibit H have been completed.

2.0 License Grant

2.1 Patent and Knowhow License Grant

(a) Genentech grants to Connetics an exclusive license, even as to Genentech, under Genentech Patent Rights and under Genentech Knowhow to use, sell, offer

for sale and import (but not to make or have made) Licensed Products in the Field of Use in the Territory, (excluding, with respect to the fields of (i) scleroderma and (ii) infectious disease or condition caused by human papillomavirus, Licensed Products containing any form of Interferon Gamma other than Genentech Gamma Interferon Δ 3, as that term is defined in the Biogen License). Notwithstanding the foregoing, Genentech reserves the right to use (but not to import, offer for sale or sell) Licensed Products within the Field of Use for research purposes.

(b) Genentech grants to Connetics a non-exclusive license under Genentech Patent Rights and under Genentech Knowhow to use, sell, offer for sale and import (but not to make or have made) Licensed Products containing any form of Interferon Gamma other than Genentech Gamma Interferon Δ 3 (as that term is defined in the Biogen License) in the Territory in the fields of: (i) scleroderma and (ii) infectious disease or condition caused by human papillomavirus.

(c) Genentech grants to Connetics a non-exclusive sublicense under the Biogen License Rights to use, sell, offer for sale and import Licensed Products (excluding Licensed Products containing Biogen Gamma Interferon Δ 0 as that term is defined in the Biogen License) in the Territory in the fields of scleroderma and infectious disease or condition caused by human papillomavirus.

(d) Genentech grants to Connetics a non-exclusive license under Genentech Patent Rights to make or have made Licensed Products in the Field of Use for use and sale in the Territory.

(e) Genentech grants to Connetics a non-exclusive license under Genentech Patent Rights and Genentech Knowhow to use non-human animal species derived

homologues of Interferon Gamma (Non-human Interferon Gamma) for non-commercial research purposes to support the Field of Use in the Territory.

Except as expressly granted herein, there are no implied licenses under the Genentech Patent Rights or any other intellectual property rights owned or controlled by Genentech.

2.2 Trademark License Grant

(a) Genentech hereby grants to Connetics a non-exclusive, royalty-free license to use the trademark, ACTIMMUNE, for the advertising, promotion, marketing, distribution and sale of Licensed Products in the Territory. Connetics shall have the right to grant sublicenses to such non-exclusive license, subject, however, to the prior written consent of Genentech,. which consent shall not be unreasonably withheld. Genentech agrees not to grant any other licenses to use the ACTIMMUNE trademark without the consent of Connetics, which consent shall not be unreasonably withheld.

(b) Use of the Mark. In using the ACTIMMUNE mark, Connetics shall display said mark in upper case letters or otherwise display it in a style or size of print distinguishing the mark from any accompanying wording or text. Where feasible, Connetics shall display the registration symbol ® to the right of and slightly above or below the last letter of the word, ACTIMMUNE. Prior to any new use by Connetics of the ACTIMMUNE mark on product packaging or package inserts for the Licensed Products, Connetics shall notify and provide Genentech with an example of the proposed use for approval by Genentech, which approval shall not be unreasonably withheld or delayed. Such additional use, with respect to the ACTIMMUNE mark, shall automatically become a part of the license grant under Section 2.2(a) above.

(c) Quality Control. If Connetics uses the ACTIMMUNE mark for Licensed Products, such products shall be of at least the quality described in the Specifications therefor as defined in the Supply Agreement.

(d) Ownership. Connetics hereby acknowledges Genentech's exclusive right, title and interest in and to the ACTIMMUNE mark and agrees that it will not at any time do, or cause to be done, any act or thing contesting or in any way impairing or intending to impair the validity of and/or Genentech's exclusive right, title and interest in and to the ACTIMMUNE mark. Connetics will not in any manner represent that it owns the ACTIMMUNE mark and hereby acknowledges that its use of the ACTIMMUNE mark as set forth in Section 2.2(b) above shall not create any rights, title or interest in or to the ACTIMMUNE mark in its favor, but that all use of the ACTIMMUNE mark by Connetics shall inure to the benefit of Genentech.

2.3 Sublicenses.

(a) Connetics may grant sublicenses under the rights granted in Section 2.1(d) on thirty (30) days prior written notice to Genentech, subject to Genentech's prior written approval, which approval shall be at Genentech's sole discretion. Genentech agrees that […***…] is acceptable to Genentech as a Connetics' sublicensee under the rights granted in Section 2.1(d) for the purpose of manufacturing and supplying Bulk Product and/or Finished Product to Connetics, and/or to its sublicensees under Sections 2.1(a), (b) and (c). In the event that Genentech approves the grant of a sublicense under Section 2.1(d), Genentech may in its sole discretion, or as agreed by the Parties in the Supply Agreement, agree to grant to Connetics and such approved sublicensee a non-exclusive license under Genentech Manufacturing Knowhow solely to make or have

made Licensed Products for use and sale by Connetics and its sublicensees in the Field of Use in the Territory, and Genentech shall thereafter disclose to Connetics and such sublicensee such Genentech Manufacturing Knowhow as soon as reasonably possible.

(b) Connetics may grant one or more sublicenses under the rights granted in Sections 2.1(a), (b), (c) and (e) in any applicable Area of the Field of Use, on thirty (30) days prior written notice to Genentech, subject to Genentech's prior written approval, which approval shall not be unreasonably withheld.

(c) Notwithstanding the above, Connetics may grant one sublicense to InterMune (as defined in Section 3.1) under any or all of the rights granted in Sections 2.1 and 2.2(a) above without Genentech's prior written approval. InterMune (but no other sublicensee of Connetics) may grant further sublicenses under Sections 2.1 and 2.2(a) to the extent that Connetics has the right to do so pursuant to the provisions of this Section 2.3 and Section 2.2(a). Connetics and InterMune shall give Genentech a copy of any sublicense agreement entered into by either of them with a third party pursuant to this Agreement as soon as reasonably possible after execution, provided that Connetics and InterMune may each redact from such copies text of information or provisions that are not relevant to this Agreement and the rights and obligations of the Parties hereunder. Genentech agrees to permit InterMune to perform Connetics' rights and obligations under Section 2.2(b), (c) and (d), Section 2.5, Sections 3.1 through 3.8 and Article 4.0 of this Agreement (excluding matters related to any alleged breach of the Agreement, or dispute between the Parties concerning the performance of this Agreement, under such enumerated Sections and Article), to the extent such rights and obligations are sublicensed to InterMune by Connetics, and Genentech agrees to deal with InterMune in lieu of Connetics as if it were Connetics

hereunder for purposes of performance under such enumerated Sections and Article, provided that Connetics shall remain liable and responsible for performance of all of the obligations of Connetics and InterMune under this Agreement. In the event that Connetics sublicenses all of its rights under Section 2.1 and 2.2(a) to InterMune pursuant to a written sublicense which provides that InterMune (and not Connetics) shall make, have made, use, sell, offer for sale, import and develop Licensed Products in all Areas of the Field of Use in the Territory, then Genentech agrees to permit InterMune to also perform Connetics' rights and obligations under Articles 5.0 and 6.0 and Sections 8.2 through 8.8 of this Agreement (excluding matters related to any alleged breach of the Agreement, or dispute between the Parties concerning the performance of this Agreement, under such enumerated Sections and Articles), and Genentech also agrees to deal with InterMune in lieu of Connetics as if it were Connetics hereunder for purposes of performance under such enumerated Sections and Articles, provided that Connetics shall remain liable and responsible for performance of all of the obligations of Connetics and InterMune under this Agreement. In the event that InterMune sublicenses any of its rights to a third party pursuant to this Agreement, such sublicensee shall not have the right to perform the rights and obligations of Connetics or InterMune under the Sections and Articles enumerated above, and Genentech shall not have any obligation to deal directly with such sublicensee. Notwithstanding the above provisions of this Section 2.3(c), with respect to any dispute concerning InterMune's performance, or alleged breach by InterMune, of any applicable term of this Agreement, Genentech shall have the right to deal directly with Connetics, and to proceed either against InterMune or directly against Connetics, in Genentech's sole discretion, to enforce this Agreement.

(d) In the event of the grant of any sublicense by Connetics (including such grant to InterMune) or by InterMune, the sublicensee shall be subject to all of the applicable obligations of Connetics hereunder. Connetics guarantees to Genentech the performance of Connetics' applicable obligations hereunder by Connetics' sublicensees and by InterMune's sublicensees.

2.4 Grant Back License. Connetics hereby grants to Genentech under any Connetics Patent Rights and Connetics Knowhow, a nonexclusive, sublicenseable license in the Territory to make, have made, use, sell, offer for sale and import Interferon Gamma for any use outside of the Field of Use, with a royalty rate of [...***...] payable to Connetics on net sales of Interferon Gamma by Genentech, its affiliates and its sublicensees covered by such Connetics Patent Rights or incorporating such Connetics Knowhow. Genentech shall have the right to grant sublicenses under such license, subject to the prior written approval of Connetics, which approval shall not be unreasonably withheld. The license granted to Genentech under this Section 2.4 shall expire on the later of: (a) the expiration of the last to expire of any Connetics Patent Rights or (b) if Connetics Knowhow was used, twenty (20) years from the first commercial sale of Interferon Gamma outside the Field of Use by Genentech, its affiliates or its sublicensees hereunder. As used herein, "net sales" shall have the equivalent definition given to Net Sales in Section 1.25 above.

2.5 Data Transfer and Cooperation

(a) Genentech shall provide Connetics with reasonable access to all such relevant information and materials in its possession (subject to Genentech's own internal reasonable needs for the information and materials) that Connetics reasonably needs to develop and commercialize Licensed Products in the Field of Use under the license granted

to Connetics under Section 2.1 above. Connetics shall submit requests for such information to Genentech's Clinical Collaborations Operations Department - Medical Affairs at the address set forth at the beginning of this Agreement. Access to such information and materials shall be made in a timely and orderly fashion and in a manner such that the value of the accessed information is preserved in all material respects.

(b) Connetics shall provide Genentech with reasonable access to such relevant information and materials in its possession as is reasonably necessary for Genentech to exercise the license rights granted by Connetics under Section 2.4 and Genentech shall submit requests for such information to Connetics' Vice President - Intellectual Property at the address set forth at the beginning of this Agreement. Access to such information and materials shall be made in a timely and orderly fashion and in a manner such that the value of the accessed information is preserved in all material respects.

(c) Commencing on May 1, 1998 Connetics or its sublicensees shall be responsible for any costs associated with maintaining the Genentech breeding colony of interferon gamma gene knock-out mice at Charles River Labs (the "Knock-Out Mice"). In consideration for Connetics paying these costs, Genentech hereby transfers all ownership of such particular Knock-Out Mice to Connetics, subject to Genentech's right to use such Knock-Out Mice and the progeny thereof for Genentech's own research purposes to the extent such Knock-Out Mice are not being used (or planned to be used) by Connetics or its sublicensees. If Connetics and its sublicensees wish to discontinue the maintenance of such Knock-Out Mice colony, Connetics shall give Genentech sixty (60) days prior notice and the right to take over such maintenance, at Genentech's sole discretion, before Connetics discontinues such maintenance. Connetics acknowledges that Genentech has, prior to the

Effective Date hereof, transferred interferon gamma gene knock-out mice to other third parties.

(d) Connetics shall use its Best Efforts to obtain a license from the FDA, which shall include obtaining a U.S. license number and an NDC number, to enable the effective transfer from Genentech to Connetics of the PLA for CGD on file with the FDA (the "CGD PLA"). Genentech shall use its Best Efforts to assist such transfer, to the extent reasonably requested by Connetics. Genentech also shall, before the Transfer Date, reasonably assist Connetics in initiating Connetics' sales of Licensed Product in the Area of the Field of Use of CGD by transferring to Connetics information reasonably requested by Connetics that relates to such sales efforts for CGD. Connetics shall reimburse Genentech for all reasonable costs associated with Genentech's providing of such information within ninety (90) days of Connetics' receipt of an invoice of such cost from Genentech.

(e) Genentech shall transfer the CGD PLA, IND and copies of all material correspondence with the FDA regarding such PLA and IND to Connetics as soon as reasonably possible after the Effective Date of this Agreement and Connetics shall be responsible for all activities, at its own cost, necessary to maintain the CGD PLA and IND and keep them active with the FDA after such date. Connetics shall reimburse Genentech for 50% of all reasonable costs associated with Genentech's transfer of the CGD PLA, IND and such FDA correspondence within ninety (90) days of Connetics' receipt of an invoice of such cost from Genentech.

(f) Connetics shall not commence marketing and sales of Finished Product prior to the Transfer Date. On the Transfer Date, Genentech shall transfer to Connetics the responsibility for all marketing and sales of Finished Product in the Field of Use in the

Territory, provided that all the activities listed on Exhibit H attached hereto are completed. The Parties shall use Best Efforts to complete the tasks set forth on Exhibit H as expeditiously as possible.

(g) Genentech shall provide Connetics with reasonable access to relevant data and regulatory information in its possession in the form existing as of the Effective Date, whether written or electronic, including all clinical safety data and clinical efficacy data that are related to the manufacture, use and sale of Interferon Gamma within the Field of Use and the right to cross-reference Genentech's IND, ELA, and PLA information for Interferon Gamma in any Genentech regulatory filings related to Interferon Gamma within the Field of Use. Other than as expressly set forth herein, Genentech shall have no further obligation with respect to Connetics' efforts to obtain the FDA license referred to in Section 2.5(d) above. At Genentech's sole discretion, Genentech may participate in regulatory filings in the Field of Use in the Territory if the Parties agree that Genentech's participation in such regulatory filings would expedite the approval and commercialization of a Licensed Product. Connetics shall reimburse Genentech for all reasonable costs associated with Genentech's providing of data and regulatory information and referencing within ninety (90) days of Connetics' receipt of an invoice of such cost from Genentech. Connetics shall submit requests for such information to Genentech's Clinical Collaborations Operations Dept. - Medical Affairs at the address set forth in the beginning of this Agreement. Such requests shall not be submitted more than two (2) times in any twelve (12) month period, unless such requests concern information that is critical to product registration activities. Access to such information shall be made in a timely and orderly fashion and in a manner such that the value of the accessed information is preserved in all material respects.

(h) To the extent reasonably requested by Genentech, Connetics shall provide Genentech with access to all data and regulatory information in its possession, whether written or electronic, in the form existing as of the date of Genentech's request, including all clinical safety data and clinical efficacy data, that directly relates to the use of Interferon Gamma outside the Field of Use and shall give Genentech the right to cross-reference Connetics' IND, ELA, BLA and PLA information, if applicable, in any Genentech regulatory filings that are related to the use or sale of Interferon Gamma outside the Field of Use. Genentech shall reimburse Connetics for all reasonable actual costs associated with Connetics' providing of data and regulatory information and referencing within ninety (90) days of the receipt of an invoice of such cost by Genentech from Connetics. Such requests shall not be submitted more than two (2) times in any twelve (12) month period, unless such requests concern information that is critical to product registration activities. Access to such information shall be made in a timely and orderly fashion and in a manner such that the value of the accessed information is preserved in all material respects.

(i) Commencing from Genentech's first delivery to Connetics or Intermune of Finished Product for clinical studies in accordance with the Supply Agreement, Connetics shall thereafter be responsible for supplying ACTIMUNE free of charge to, and funding (if any) of, the third party sponsors of the clinical studies listed in Exhibit D attached hereto and incorporated herein. Connetics shall enter into clinical research agreements with such third party sponsors governing such studies that commence after the Effective Date hereof. With respect to clinical research agreements between Genentech and such sponsors in effect prior to the Effective Date, Connetics shall replace Genentech, pursuant to an

assignment, as a party. ACTIMMUNE (and funding, if any) for all such studies shall be supplied by Connetics to such sponsors as described in such clinical research agreements.

(j) As of the Transfer Date, Connetics shall conduct an indigent patient program for Licensed Products sold for use in the field of CGD. As soon as reasonably possible after Genentech transfers information regarding patients who have participated in Genentech's indigent patient program, Connetics will inform Genentech whether or not such patients will be eligible and participating in Connetics' indigent patient program.

3.0 Product Development and Milestones

3.1 Commercialization Milestones.

(a) Connetics shall use its Best Efforts to develop, seek FDA clearance for marketing of, commercialize and sell Licensed Products in the Territory in all Areas of the Field of Use. The Parties acknowledge that a new company, named InterMune Pharmaceuticals, Inc. ("InterMune"), has been incorporated to conduct development and commercialization of Licensed Products in the Field of Use pursuant to an appropriate sublicense from Connetics to Intermune. Connetics agrees to perform the following Commercialization Milestones no later than the date set forth below opposite the appropriate Commercialization Milestone description:

Commercialization Milestone	Date of Completion
(a) Completion of the formation of InterMune	May 1, 1998
(b) Execution of a sublicense agreement granting to InterMune rights, as permitted in this Agreement,	June 1, 1998

necessary to perform development of Licensed Products in the Field	
(c) Closing of at least […***…] in equity financing of InterMune by third parties and/or Connetics	July 15, 1998
(d) Closing of at least another additional […***…] in equity financing of InterMune by third parties and/or Connetics	September 1, 1998
(e) Enrollment and active participation of the first patient in the first new clinical trial for a Licensed Product in the Field of Use in the Territory	October 1, 1998

(b) If Connetics fails to perform any of the Commercialization Milestones described in 3.1 (a) through (e) inclusive by the applicable Date of Completion for any reason within Connetics' control, then, notwithstanding the termination provisions in Section 11.2 below, Genentech shall have the right to terminate this Agreement and the licenses granted to Connetics hereunder, upon written notice to Connetics, which termination shall become effective thirty (30) days after Genentech's sending written notice of such termination, unless such Commercialization Milestone has been completed prior to the expiration of such thirty day period. If Connetics fails to perform any of the Commercialization Milestones for causes beyond Connetics' control, Genentech shall not have the termination rights above, provided that Connetics has mitigated such causes to the extent it can reasonably do so. If Connetics fails to reasonably mitigate such causes, Genentech will have the termination rights described above. In addition, if Genentech

exercises such termination rights above, Genentech shall be automatically granted a co-exclusive (with Connetics and Connetics' sublicensees), sublicenseable, royalty-free, worldwide license: (i) to the result of efforts made by Connetics and its sublicensees in the development of Licensed Products hereunder, (ii) to use all regulatory submissions made by Connetics and its sublicensees hereunder, and (iii) under all Connetics Patent Rights and Connetics Knowhow, arising from the efforts made by Connetics and its sublicensees hereunder in the research and development of Licensed Products, to make, have made, use, sell, offer for sale or import Licensed Products. Upon Genentech's exercise of such termination right described above, Connetics shall promptly provide Genentech with copies of all related documentation, whether written or electronic, and materials, including biological materials, in the form existing as of the effective date of such termination, reasonably necessary for Genentech to exercise its license rights under this Section 3.1(b). Such transfer shall be made in an orderly fashion and in a manner such that the value in what is being transferred is preserved in all material respects. The foregoing shall constitute Genentech's exclusive remedies for Connetics failure to complete one or more of the Commercialization Milestones above, provided, however, that Genentech's rights and remedies for breach of other provisions of this Agreement, and under the Supply Agreement and the Stock Agreement, shall remain in full force and effect.

3.2 Diligence

(a) Attached hereto as Exhibit E are Connetics' Clinical Development Milestones (the "Clinical Development Milestones") for Licensed Products in the Field of Use and the Dates of Completion for each such milestone. Connetics shall use its Best

Efforts to adhere to the Dates of Completion as set forth in Exhibit E. Connetics shall notify Genentech in writing when it achieves a Clinical Development Milestone.

(b) From time to time, Connetics may suggest modifications to the Clinical Development Milestones based on new information. Such modifications shall be effective only as mutually agreed upon, in writing, by the Parties. Genentech shall consider such requested modifications in good faith and shall agree to any modifications that are reasonably necessary to achieve the overall objectives of the development of Licensed Product hereunder.

(c) In the event that Connetics determines that it will be unable to meet any Date of Completion for a Clinical Development Milestone due to an event within Genentech's control, including without limitation, delay in the performance by Genentech of any of its obligations hereunder (e.g. the transfer of technology or materials, including the supply of Interferon Gamma-1B), Connetics shall give prompt notice to Genentech of such inability and shall specify the amount of delay Connetics believes resulted from such event within Genentech's control. Unless Genentech disagrees in writing on reasonable grounds with the amount of such delay specified by Connetics, such Date of Completion will automatically be extended by the length of time of the delay. In the event Genentech disagrees in writing on reasonable grounds with the amount of delay specified by Connetics, the Parties shall negotiate a new Date of Completion in good faith.

(d) In the event that Connetics determines that it will be unable to meet any Date of Completion for a Clinical Development Milestone due to an event which would be considered a force majeure (as described in Section 12.9), Connetics shall give prompt written notice to Genentech of such inability and the length of the delay Connetics believes

resulted from such force majeure. Unless Genentech disagrees in writing on reasonable grounds with the length of such delay specified by Connetics, such Date of Completion will be automatically extended by such specified length of time of the delay. In the event Genentech disagrees in writing on reasonable grounds with the length of delay specified by Connetics, the Parties shall negotiate a new Date of Completion in good faith.

(e) In the event that Connetics determines that it will be unable to meet any Date of Completion for a Clinical Development Milestone for reasons other than (i) force majeure and/or (ii) an event within Genentech's control, Connetics shall notify Genentech of such inability, identifying the nature of the inability with reasonable specificity and may ask Genentech for a reasonable extension of time in which to complete such Clinical Development Milestone. In Genentech's sole discretion, Genentech may grant Connetics such an extension to complete such Clinical Development Milestone.

(f) Except as set forth in Sections 3.2(c) or 3.2(d) or in the event that Genentech shall have agreed to an extension of the time to complete a Clinical Development Milestone as set forth in Section 3.2(e), if Connetics fails to complete a Clinical Development Milestone by the corresponding Date of Completion with respect to one or more of the Areas of the Field of Use (other than in the dermatological Area of the Field of Use as described in Section 1.12(a) above) Genentech shall have the right to terminate this Agreement with respect to such Area(s) of the Field of Use, by providing Connetics written notice thereof, and the termination of the Agreement with respect to such Area(s) of the Field of Use shall be effective thirty (30) days after Connetics' receipt of such notice unless such Clinical Development Milestone shall have been met prior to the expiration of such thirty (30) day period, and such termination shall be Genentech's exclusive remedy for such failure

of Connetics to complete such Clinical Development Milestone. Upon such termination of the Agreement with respect to such Area(s) of the Field of Use: (i) Genentech shall automatically have all the rights set forth in Sections 11.3(a) and (b) solely with respect to such Area(s) of the Field of Use; and (ii) any sublicense(s) granted by Connetics with respect to such Area(s) of the Field of Use shall not automatically terminate, but instead, Genentech shall have the option to either terminate or continue this Agreement with respect to such Area(s) of the Field of Use with such sublicensee(s).

3.3 Review of Clinical Development Plan and Marketing Programs. On or about each August 1 during the term of this Agreement, Connetics shall supply Genentech with a report on Connetics' development and marketing programs for Licensed Products in the Field of Use in the Territory. The report shall include the following: (i) a description of Connetics' progress in such programs during the twelve (12) months prior to the date of each such report, (ii) a description of Connetics' planned development and marketing programs for the twelve (12) months after the date of each such report, (iii) a copy of the most recent version of the Clinical Development Milestones (if not previously provided to Genentech), (iv) a copy of all previous versions of the Clinical Development Milestones (if not previously provided to Genentech), (v) an explanation of any discrepancies between Connetics' progress during the prior twelve (12) months and the Clinical Development Milestones and (vi) a proposal to address such discrepancies, as contemplated under Section 3.2. Genentech shall have the right to comment on the Clinical Development Milestones and the development and marketing programs,. and at Genentech's -discretion, the Parties shall meet to discuss and agree upon changes to the Clinical Development Milestones.

3.4 New Delivery Forms. Connetics shall have the right to develop and obtain regulatory approval for the marketing of new delivery forms of Interferon Gamma for use in Licensed Products in the Field of Use in the Territory.

3.5 Costs of Development. Connetics shall be responsible for all aspects and costs of development, regulatory approval and registration of Licensed Products.

3.6 Joint Development and Marketing Activities. Upon written notice to Genentech, Connetics and InterMune shall be permitted to discuss and enter into agreements and participate in joint development and marketing activities for Licensed Products in the Field of Use outside the Territory with other Genentech Interferon Gamma licensees.

3.7 Compliance with Law and Safety and Adverse Event Reporting.

(a) Connetics shall conduct clinical trials hereunder, and shall make, use, sell and distribute Licensed Products in accordance with all applicable laws and regulations. Genentech and Connetics shall make available to each other during the term of this Agreement all safety data obtained which relates to the use of Licensed Products in the Field of Use. Connetics will provide to Genentech's Medical Information and Drug Experience department at the time of filing a copy of each adverse event report or any report, including summary reports, it is required to file under Title 21 or any other applicable provision of the C.F.R. regarding Interferon Gamma. Genentech will provide Connetics at the time of filing with a copy of each adverse event report or any report, including summary reports, it is required to file regarding Interferon Gamma under Title 21 or any other applicable provision of the C.F.R..

(b) Connetics shall maintain a safety database for all Licensed Products and clinical trials conducted hereunder and shall submit to regulatory agencies all adverse

event and safety reports required to be filed pursuant to Title 21 or any other applicable provision of the C.F.R. Connetics shall also be responsible for providing product, medical and clinical information regarding Licensed Product to its customers.

3.8 Clinical Development Reports. During the course of clinical development of Licensed Products and clinical studies conducted by Connetics hereunder, Connetics shall submit to Genentech the reports listed on Exhibit F attached hereto and incorporated herein. Connetics shall submit such reports to Genentech as promptly as reasonably practicable after such reports are completed or such applicable information is available.

3.9 Technology Outside the Field of Use

(a) Upon mutual written amendment to this Agreement, the Parties may expand the Field of Use, subject to the terms and conditions for supply of Interferon Gamma 1-B set forth in the Supply Agreement, the payments set forth in Sections 8.2 through 8.8 below inclusive and all other applicable obligations of Connetics under this Agreement.

(b) Connetics may request an expansion of the Field of Use in the Territory, by providing Genentech with a written letter of intent which incorporates the terms and conditions specified in the Supply Agreement and Sections 8.2 through 8.8 of this Agreement and sets forth a detailed clinical development plan and reasonable proposed timeline (through FDA clearance) for developing the additional medical indication(s) sought. Such letter of intent shall be deemed Confidential Information of Connetics. Upon receipt of such letter of intent, unless Genentech is conducting research in, or developing, Interferon Gamma for such specified use, is already engaged in negotiations with a third party for such specified use, or is prevented by prior written agreements to grant rights to such additional indications to Connetics, Genentech shall negotiate exclusively in good faith with Connetics,

for a period of sixty (60) days on a one time basis only for each such new indication outside the Field of Use, to expand the Field of Use as proposed in the letter of intent on terms substantially similar to those contained in this Agreement. If the Parties do not reach mutual written agreement with respect to such proposed expansion of the Field of Use within sixty (60) days, Genentech shall continue to have the right to license its rights to such proposed additional indications for Interferon Gamma outside the Field of Use to third parties other than Connetics, provided that, for a period of six (6) months after the 60 day exclusive negotiation period with Connetics, the milestone fee and royalty terms offered by Genentech to third parties for such indications are not more favorable to such third parties than those in the final offer made by Connetics.

(c) Prior to offering any third party an opportunity to obtain any right or license under Genentech Patent Rights, Genentech Knowhow, or Biogen License Rights to use, sell, offer for sale or import Licensed Products for any indication outside the Field of Use in the Territory, Genentech shall first offer to Connetics to expand the Field of Use to include such indication, in accordance with Section 3.8(d) below. Such obligation to first offer to Connetics such indication outside the Field of Use shall apply only to the first time Genentech wishes to offer rights to another party to such indication outside the Field of Use.

(d) Genentech may offer to expand the Field of Use by written notice to Connetics ("Offer Notice"). Upon receipt of such Offer Notice, Connetics shall have thirty (30) days to provide Genentech with a written letter of intent which incorporates the terms and conditions specified in the Supply Agreement and Sections 8.2 through 8.8 of this Agreement. Upon receipt of such letter of intent, Genentech shall negotiate exclusively in good faith with Connetics, for a period of thirty (30) days on a one time basis only for each

such new indication outside the Field of Use, to expand the Field of Use as proposed in the letter of intent on terms substantially similar to those contained in this Agreement. If the Parties do not reach mutual written agreement with respect to such proposed expansion of the Field of Use within 30 days, Genentech shall continue to have the right to license its rights to such proposed additional indications for Interferon Gamma outside the Field of Use to third parties other than Connetics. To remain under consideration as a potential licensee for such rights to Interferon Gamma outside the Field of Use, within ninety (90) days of receipt of Genentech's Offer Notice, Connetics shall provide Genentech with a detailed written clinical development plan and reasonable proposed timeline for developing (through FDA clearance) the additional medical indication(s) sought, which development plan shall be deemed the Confidential Information of Connetics.

4.0 Supply of Interferon Gamma-1B

4.1 Bulk Product and Finished Product. Genentech shall supply Connetics with, and Connetics shall purchase, Bulk Product for clinical studies and for sales of Licensed Product and Finished Product for commercial sale of Licensed Product to treat CGD and osteopetrosis and for clinical studies, pursuant to the terms and conditions of the Supply Agreement.

4.2 Supply of Non-human Interferon Gamma. Upon Connetics' reasonable request and in Genentech's sole discretion, Genentech may choose to sell to Connetics Non-human Interferon Gamma at a price equal to […***…]. Notwithstanding the foregoing, Genentech shall have no obligation to (a) provide any minimum amount of Non-human Interferon

Gamma to Connetics or (b) produce additional amounts of Non-human Gamma Interferon in the event its current inventory is depleted.

5.0 Intellectual Property Rights

5.1 Ownership. Genentech shall retain title to Genentech Patent Rights, Genentech Knowhow, Genentech Manufacturing Knowhow, the ACTIMMUNE mark, and to any patent rights and knowhow related to Interferon Gamma or Licensed Products developed solely by Genentech. Connetics shall retain title to Connetics Patent Rights and Connetics Knowhow and to any patent rights and knowhow related to Interferon Gamma and Licensed Products developed solely by Connetics. Except as expressly provided herein, each Party shall own and shall have the exclusive right to exploit all intellectual property rights owned or acquired by such Party.

5.2 Patent Prosecution and License Fees

(a) With the exception of Genentech Patent Rights under the […***…] License, Genentech shall be responsible for the prosecution and maintenance of the Genentech Patent Rights in the Territory at Genentech's expense, in consultation with Connetics. Genentech shall be responsible for the prosecution and maintenance and outside counsel fees associated therewith of the Genentech Patent Rights under the […***…] License in the Field of Use in the Territory at Connetics' expense, upon prior consultation with and approval from Connetics, which approval shall not be unreasonably withheld or delayed. Genentech shall keep Connetics promptly informed of the status of prosecution of Genentech Patent Rights in the Territory, including providing copies of all material correspondence with the U.S. Patent and Trademark Office. Connetics shall have the right to comment upon such

prosecution and Genentech agrees to take such comments into consideration reasonably in advance of any action taken by Genentech in such prosecution.

(b) Connetics shall assist Genentech in prosecuting and maintaining the Genentech Patent Rights as contemplated by Section 5.2(a) above.

(c) At least thirty (30) days prior to the time each benchmark payment of […***…] under the […***…] License becomes due during the term of this Agreement, Genentech shall notify Connetics of such payment due and Connetics shall have the option of paying such benchmark payment, on Genentech's behalf, when due to […***…]. In the event that Connetics chooses not to pay the benchmark payment when due, Connetics shall so notify Genentech and Genentech shall have the option of paying such benchmark payment. If Genentech pays such benchmark payment, Connetics shall reimburse Genentech for such payment within thirty (30) days of receipt of Genentech's request for reimbursement.

5.3 Patent Infringement

(a) If either Party learns that a third party is infringing Genentech Patent Rights or Connetics Patent Rights, it shall promptly notify the other in writing. The Parties shall use reasonable efforts in cooperation with each other to stop such patent infringement without litigation.

(b) Genentech and Connetics each shall have the first opportunity to take the appropriate steps to remove the infringement of its own Patent Rights which claim Interferon Gamma and/or its manufacture or use in the Field of Use including, without limitation, initiating suit. In either case, if such Party decides not to take such steps with respect to its own Patent Rights within one hundred twenty (120) days of discovering or being notified of the infringement, the other Party may do so. Each of the Parties agrees to

provide reasonable assistance to the other in taking such steps. Any legal action taken under this section will be at the expense of the Party by whom suit is filed and will be controlled by the Party bringing suit. The Party not bringing suit may choose to be represented in any such action by counsel of its own choice at its own expense. The Party bringing suit shall be reimbursed for its costs associated with bringing suit with the proceeds of any damages or costs recovered. Any monies remaining shall be split between the Parties on an equitable basis proportional to their respective damage from the infringement. If both Parties bring suit, equitable apportionment of the costs and damages to be recovered shall be agreed upon before the filing of the suit.

5.4 Third Party Rights. If a notice of infringement is received by, or a suit is initiated against, either of Connetics or Genentech with respect to Licensed Products or the ACTIMMUNE mark, the Parties will in good faith discuss the best way to respond.

5.5 Trademark Infringement

(a) If either Party learns that a third party is infringing the ACTIMMUNE mark, it shall promptly notify the other in writing. The Parties shall use reasonable efforts in cooperation with each other to stop such trademark infringement without litigation.

(b) Genentech shall have the first opportunity to take the appropriate steps to remove the infringement of the ACTIMMUNE mark, including, without limitation, initiating suit. If Genentech decides not to take such steps within one hundred twenty (120) days of discovering or being notified of the infringement, Connetics may do so. Each of the Parties agrees to provide reasonable assistance to the other in taking such steps. Any legal action taken under this section will be at the expense of the Party by whom suit is filed and will be controlled by the Party bringing suit. The Party not bringing suit may choose to be

represented in any such action by counsel of its own choice at its own expense. The Party bringing suit shall be reimbursed for its costs associated with bringing suit with the proceeds of any damages or costs recovered. Any monies remaining shall be split between the Parties on an equitable basis proportional to their respective damage from the infringement. If both Parties bring suit, equitable apportionment of the costs and damages to be recovered shall be agreed upon before the filing of the suit.

5.6 […***…] License. If Genentech receives notice that it has acquired any Genentech Patent Rights under the […***…] License after the Effective Date of this Agreement, Genentech shall notify Connetics in writing of such additional rights as soon as reasonable after Genentech receives such notice.

6.0 Product Promotion

6.1 Promotion. Genentech agrees, and shall require its sublicensees, if any, to agree, not to promote Interferon Gamma or a Licensed Product in the Field of Use in the Territory. Connetics agrees, and shall require its sublicensees to agree, not to promote Interferon Gamma or a Licensed Product outside the Field of Use or outside the Territory.

6.2 Encroachment. In the event that either Party becomes aware of spillover sales of Interferon Gamma by Genentech that is used within the Field of Use or of Licensed Product by Connetics that is used outside the Field of Use, the Parties, shall meet and agree in good faith on reasonably appropriate steps (a) to abate such encroachment and (b) to compensate the Party which has suffered encroachment in its field of use by such spillover sales.

7.0 Confidentiality

In the course of performance of this Agreement, one Party may disclose to the other or receive information from the other relating to the subject matter of this Agreement which information shall be considered to be the disclosing Party's confidential. information, if in the case of a written disclosure, it is designated as confidential at the time of disclosure, or if in the case of oral disclosure, the specific nature of the oral disclosure and its confidentiality is confirmed in writing to the other Party within thirty (30) days of the oral disclosure (the "Confidential Information"). Each Party shall protect and keep confidential and shall not use, publish or otherwise disclose to any third party, except as permitted by this Agreement or with the other Party's written consent, the other Party's Confidential Information for a period of five (5) years from the date of termination of this Agreement if it is terminated at any time within five (5) years after the Effective Date of this Agreement, otherwise for a period of three (3) years from date of termination or expiration of this Agreement. A Party may disclose the other Party's Confidential Information to its sublicensees hereunder, provided that such sublicensees are subject to obligations of confidentiality at least equivalent to those set forth in this Article 7. The Parties shall consult prior to the submission of any manuscript for publication to determine if the publication will contain any Confidential Information of the other Party. Such consultation shall include providing a copy of the proposed manuscript to the other Party at least forty-five (45) days prior to the proposed date of submission to a publisher, incorporating appropriate changes proposed by the other Party into the manuscript submission and deleting all of the other Party's Confidential Information which such Party does not agree to the publication thereof. The foregoing notwithstanding, Confidential Information may be disclosed: (a) during any

official proceeding before a court or governmental agency if reasonably related to that proceeding; (b) as a part of a patent application filed on inventions made under this Agreement, provided that the Party whose Confidential Information is included in such application shall have the opportunity to review such disclosure at least fifteen (15) business days prior to the date of such filing and such Party does not object to such disclosure; and (c) as may be reasonably required to comply with applicable governmental laws or regulations. For the purposes of this Agreement, Confidential Information shall not include such information that:

(i) was known to the receiving Party at the time of disclosure;

(ii) was generally available to the public or was otherwise part of the public domain at the time of disclosure or became generally available to the public or otherwise part of the public domain after disclosure other than through any act or omission of the receiving Party in breach of this Agreement;

(iii) became known to the receiving Party after disclosure from a source that had a lawful right to disclose such information to others; or

(iv) was independently developed by the receiving Party without the use of Confidential Information of the other Party, as evidenced by written records.

If Connetics sublicenses any of its rights hereunder to InterMune pursuant to this Agreement, Genentech and InterMune shall enter into a mutual confidentiality agreement, substantially in the form of this Article 7.0, to protect confidential information that may be disclosed by InterMune to Genentech.

8.0 Up-front Payment, Milestone Payments and Royalties

In consideration for the licenses granted to Connetics by Genentech pursuant to Section 2.0 above, Connetics shall make the following payments to Genentech:

8.1 Up-front Payment. Connetics shall issue to Genentech upon the Original Closing Date (as defined in the Stock Agreement) shares of Connetics Common Stock ("Original Issuance Shares" as defined in the Stock Agreement) with a fair market value equal to two million dollars ($2,000,000), on the terms and conditions set forth in the Stock Agreement. If, on the Second Closing Date (as defined in the Stock Agreement), the aggregate market value of the Original Issuance Shares (based on the Second Issuance Price (as defined in the Stock Agreement)) is less than four million dollars ($4,000,000), Connetics shall issue to Genentech upon the Second Closing Date the number of additional shares of Connetics Common Stock (the °Second Issuance Shares," as defined in the Stock Agreement) equal to the lesser of: (i) the number of shares necessary to increase the aggregate market value of the Original Issuance Shares (based on the Second Issuance Price) plus the Second Issuance Shares (based on the Second Issuance Price) to four million dollars ($4,000,000) or (ii) the number of shares necessary to increase the aggregate number of the Company's shares of Common Stock held by Genentech (exclusive of any shares that Genentech has purchased from parties other than the Company) to 9.9% of the Company's total outstanding shares of Common Stock as of the close of business on the third trading day before the Second Closing Date, on the terms and conditions set forth in the Stock Agreement. In lieu of all or any portion of the Second Issuance Shares that the Company is obligated to issue to Genentech on the Second Closing Date, the Company may elect to pay

Genentech the cash value of such Second Issuance Shares (based on the Second Issuance Price). The Original Closing and the Second Closing of the stock issuances shall take place as described in the Stock Agreement. In the event that Connetics does not issue to Genentech all of the Second Issuance Shares or the cash value of the Second Issuance Shares, Genentech may, in addition to other remedies available to it by law or in equity, immediately terminate this Agreement and the licenses granted to Connetics hereunder. Such termination by Genentech of the Agreement and the licenses hereunder does not discharge Connetics' obligation to issue all of the Second Issuance Shares or to pay to Genentech the cash value of the Second Issuance Shares. The up-front payment shall not be creditable against any royalty payments owed by Connetics under Sections 8.3 and 8.4 below.

8.2 Milestone Payments for Licensed Products. Connetics shall make the following cash milestone payments to Genentech:

(a) […***…] within thirty (30) days following the dates on which each of the first three (3) NDA's or BLA's for a Licensed Product is filed with the FDA by Connetics for a new indication in the Field of Use; provided however, that such milestone payments shall not be paid upon the filing of a NDA or BLA for an osteopetrosis or atypical mycobacterial infection indication.

(b) […***…] within thirty (30) days following the date Connetics receives FDA clearance of each new indication for a Licensed Product for commercial sale in the United States; provided however, that such milestone payment shall not be paid upon receipt of FDA clearance for an osteopetrosis or atypical mycobacterial infection indication.

(c) […***…] within thirty (30) days following the first date Connetics' aggregate Net Sales of all Licensed Products in the Territory exceed […***…] in any calendar year.

(d) […***…] within thirty (30) days following the first date Connetics' aggregate Net Sales of all Licensed Products in the Territory exceed […***…] in any calendar year.

Notwithstanding the foregoing, upon the expiration or revocation of the last remaining issued patent within the Genentech Patent Rights during the term of this Agreement, each of the milestones payments set forth in (a)-(d) above thereafter shall be reduced by fifty percent (50%). Milestone payments shall not be creditable against any royalty payments owed under Sections 8.3 and 8.4 below.

8.3 Royalties. Connetics shall pay Genentech the following royalties on Net Sales of Licensed Products by Connetics and its sublicensees:

(a) For annual aggregate Net Sales of all Licensed Products in the Territory of up to three million seven hundred thousand dollars ($3,700,000), a royalty rate equal to 45% of such Net Sales.

(b) In addition to the payment of the royalty rate specified in (a) above, for annual aggregate Net Sales of all Licensed Products in the Territory exceeding three million seven hundred thousand dollars ($3,700,000), a royalty rate equal to […***…] of such Net Sales exceeding $3,700,000.

(c) The above royalties shall be payable until the later of: (i) the expiration or revocation of the last remaining issued patent within the Genentech Patent Rights or (ii) twenty (20) years from the Effective Date of this Agreement. Notwithstanding the

foregoing, upon the expiration of the last to expire issued patent within the Genentech Patent Rights during the term of this Agreement, thereafter each of the royalty rates set forth in (a) and (b) above shall be reduced by fifty percent (50%).

8.4 Third-Party Royalties. If Genentech or Connetics is required to pay any third party a royalty due to the manufacture, use, sale, offer for sale or importation of a Licensed Product in the Territory for or by Connetics or its sublicensees, Connetics shall be responsible for the payment of […***…] of such third-party royalty, provided however, that Connetics may deduct from the royalties payable to Genentech under Section 8.3 above […***…] of such third party royalties incurred only due to use patents in the Field of Use in the Territory, up to a maximum total deduction of […***…] percentage points from the royalties payable by Connetics to Genentech under Section 8.3. For purposes of clarification, such deductions shall not apply to any benchmark payment under the […***…] License made by Connetics pursuant to Section 5.2(c) above. Attached hereto as Exhibit G is a list of all such royalty obligations to third parties known to Genentech as of the Effective Date without diligent search. No later than thirty (30) days from the Effective Date, Genentech shall complete a reasonable internal investigation of its records and update Exhibit G, as necessary, to accurately reflect all such royalty obligations to third parties to the best of Genentech's knowledge; provided however, Connetics acknowledges that Genentech has no obligation to conduct due diligence or any investigation with respect to third party patent rights related to Licensed Products. Genentech shall notify Connetics in writing during the term of this Agreement if it becomes aware of any additional Genentech third party royalty obligations.

8.5 Royalty Payments. Royalty payments shall be made to Genentech quarterly within ninety (90) days following the end of each calendar quarter for which royalties are due. Each royalty payment shall be accompanied by a report summarizing the total Net Sales during the relevant three-month period, and the calculation of royalties, if any, due thereon pursuant to Section 8.3.

8.6 Taxes. Genentech shall pay any and all taxes levied on account of, or measured by, any payment, including, without limitation, royalties, it receives under this Agreement.

8.7 Termination. If the license granted to Connetics herein is terminated by the Parties, Connetics shall have no obligation to make any milestone or royalty payments to Genentech that has not accrued prior to the effective date of such termination, but shall remain liable for all such payments accruing prior to termination.

8.8 Records and Reporting Records.

(a) Connetics and any sublicensee of Connetics shall keep full, true and accurate books of account containing all particulars which may be necessary for the purpose of showing Net Sales. Said books of account shall be kept at the principal place of business of Connetics or its sublicensee, as the case may be. Said books and the supporting data shall be open at all reasonable times, for three (3) years following the end of the calendar year to which they pertain (and access shall not be denied thereafter, if reasonably available), to the inspection of an independent public accountant retained by Genentech and reasonably acceptable to Connetics (or its sublicensee) for the purpose of verifying Net Sales under this Agreement; subject to the provisions of Section 8.8(c) below.

(b) Reports. Connetics shall within ninety (90) days after the end of each calendar quarter beginning with the quarter of the first commercial sale of Licensed Product in the Field of Use in the Territory by Connetics or its sublicensee, deliver to Genentech a true and accurate report, setting forth such particulars of the business conducted by Connetics and its sublicensees during the preceding quarter as are pertinent to an accounting for Net Sales and deductible expenses under this Agreement. Such reports shall include at least the following: (i) the total gross sales of Licensed Products occurring during that calendar quarter, (ii) the allowable deductions therefrom, (iii) the total Net Sales of Licensed Products occurring during that calendar quarter and (iv) the calculation of royalties, if any, due thereon pursuant to the above Section 8.3.

(c) Auditing. At Genentech's request and expense, Connetics shall permit a certified public accountant selected by Genentech and acceptable to Connetics to examine, not more than once in any four consecutive calendar quarters during the term of this Agreement, but including one (1) post-termination audit, Connetics' books of account and records of all sales of Licensed Products by Connetics for the sole purpose of determining the correctness of the reports provided by Connetics under the above Section 8.8(b). If such accountant reasonably determines that the royalties owed by Connetics to Genentech under the above Section 8.3 have been, for any calendar year in total, understated by Connetics, Connetics shall immediately pay all understated royalties, together with interest on such royalties from the date accrued at a rate of […***…] and shall pay the reasonable costs of the examination if Connetics has understated such royalties by more than [...***...].

9.0 Representations and Warranties

9.1 Disclaimer. Except as expressly provided herein, the Parties disclaim all other representations and warranties, express or implied, including without limitation, WARRANTIES OF COMMERCIAL UTILITY, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OR SCOPE OF GENENTECH PATENT RIGHTS or NON-INFRINGEMENT OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS.

9.2 Representations and Warranties.

(a) Each party represents and warrants to the other that: (a) it is free to enter into this Agreement; (b) in so doing it will not violate any other agreement to which it is a party; (c) it is currently capable of making the grant of rights described in Sections 2.1(a), (b), (c), (d), 2.2 and 2.4; and (d) it will not enter into any agreement in the future which conflicts with or violates any term or provision of this Agreement. Genentech makes no representation or warranty that all intellectual property rights necessary for Connetics to make, have made, use, sell, offer for sale and import Licensed Products in the Field of Use in the Territory have been granted to Connetics under Section 2.0 of this Agreement.

(b) Connetics further represents and warrants that, prior to the Effective Date of this Agreement, Connetics' officers (acting under delegated authority of its Board of Directors) have determined that the fair market value of the exclusive license granted to Connetics hereunder is less than $15,000,000 and therefore that the execution and delivery of this exclusive license Agreement, or the performance .of the obligations by Genentech or Connetics hereunder, do not require that filings be made under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, or under the rules or regulations promulgated

thereunder, by Connetics, Genentech, or their respective affiliates or ultimate parent entities, if any.

(c) Genentech represents and warrants to Connetics that as of the Effective Date: (i) to Genentech's knowledge, it has not received any notice of a claim by a third party for infringement of such third party's intellectual property relating to the use and practice of the Genentech Knowhow, the Genentech Manufacturing Knowhow, the Genentech Patent Rights or the Biogen License Rights; and (ii) to the knowledge of Genentech's patent counsel, there is no issued patent that would be infringed by the practice of the Genentech Knowhow, the Genentech Manufacturing Knowhow or the Genentech Patent Rights as permitted under the license rights granted under Section 2.1; and (iii) it has no knowledge of any actual infringement by any third party in the Field of Use in the Territory of the Genentech Patent Rights.

10.0 Liability

10.1 Limitation of Liability. Neither Party shall be liable to the other for indirect, incidental, special or consequential damages arising out of any of the terms or conditions of this Agreement or with respect to their performance or lack thereof.

10.2 Connetics Indemnification. Connetics shall indemnify, defend and hold harmless Genentech and its affiliates from and against all third party costs, claims, suits, expenses (including reasonable attorneys' fees) and damages arising out of or resulting from: (a) any willful or negligent act or omission by Connetics relating to the subject matter of this Agreement or (b) the use by or administration to any person of a Licensed Product, Bulk Product or Finished Product that was sold, distributed or otherwise provided to a third party by Connetics or its sublicensees under this Agreement; except where such costs, claims, suits, expenses or damages arose or resulted from any negligent act or omission by

Genentech or any defect in the manufacture of Bulk Product or Finished Product by Genentech that was not discovered by Connetics, provided that Genentech gives reasonable notice to Connetics of any such claim or action, tenders the defense of such claim or action to Connetics and assists Connetics at Connetics' expense in defending such claim or action and does not compromise or settle such claim or action without Connetics' prior written consent.

10.3 Genentech Indemnification. Genentech shall indemnify, defend and hold harmless Connetics, its affiliates and sublicensees from and against all third party costs, claims, suits, expenses (including reasonable attorney's fees) and damages arising out of or resulting from: (a) any willful or negligent act or omission by Genentech relating to the subject matter of this Agreement; (b) any defect in the manufacture of Bulk Product or Finished Product by Genentech that was not discovered by Connetics; or (c) the use by or administration to any person of a product containing Interferon Gamma sold, distributed or otherwise provided to a third party by Genentech or its sublicensees; except where the foregoing costs, claims, suits, expenses or damages arose or resulted from (i) any negligent act or omission by Connetics or (ii) the use by or administration to any person of a Licensed Product sold, distributed or otherwise provided by Connetics or its sublicensees other than resulting from a defect in the manufacture of such Licensed Product by Genentech, provided that Connetics gives reasonable notice to Genentech of any such claims or action, tenders the defense of such claim or action to Genentech and assists Genentech at Genentech's expense in defending such claim or action and does not compromise or settle such claim or action without Genentech's prior written consent.

11.0 Term and Termination

11.1 Term. This Agreement shall commence on the Effective Date of this Agreement and, unless terminated earlier, shall expire at the later to occur of (a) the expiration of the last to expire of any Genentech Patent Rights or (b) twenty (20) years from the Effective Date of this Agreement; provided, however, that in the event that either the […***…] License or the Biogen License is terminated, the licenses granted by Genentech to Connetics under the […***…] License or the Biogen License shall also terminate. Genentech shall use its Best Efforts to keep the […***…] License and the Biogen License in effect during the term of this Agreement, provided, however, that if Connetics declines to pay a […***…] benchmark payment as outlined in Section 5.2(c) or pay any royalty owed to […***…] under the […***…] License for the sales of Licensed Products, then Genentech shall not be obligated to make such payment and Genentech shall have the option, in its sole discretion, to terminate the […***…] License. One year before the expiration of this Agreement under this Section 11.1, the Parties agree to meet and to discuss in good faith extending the term of this Agreement on terms mutually agreeable to the Parties.

11.2 Termination for Default. If either Party shall default in a material manner with respect to any material provision of this Agreement and the other Party shall have given the defaulting Party written notice of such default, the defaulting Party shall have thirty (30) days to cure such default. If such default is not cured within such thirty (30) day period, the non-defaulting Party shall have the right, upon notice to the defaulting Party and without prejudice to any other rights the non-defaulting Party may have, to terminate this Agreement unless the defaulting Party is in the process of attempting in good faith to remedy such default, in which case, the thirty (30) day cure period shall be extended by an additional thirty (30) days. If Genentech terminates this Agreement pursuant to this Section 11.2,

Genentech shall automatically have all of the rights set forth in Sections 11.3(a) and (b) of this Agreement. Upon such termination, any sublicenses granted under this Agreement shall not automatically terminate, but instead, Genentech shall have the option to either terminate or continue this Agreement with each sublicensee. If Connetics terminates this agreement pursuant to this Section 11.2, Connetics shall automatically have all of the rights set forth in Section 11.4 of this Agreement. Connetics shall have no right to terminate this Agreement pursuant to this Section 11.2 in the event of Genentech's failure to supply Bulk Product or Finished Product. In the event of Genentech's failure to supply Bulk Product or Finished Product, Connetics shall have the rights set forth in the Supply Agreement.

11.3 Genentech's Rights on Termination

(a) If Genentech terminates this Agreement pursuant to Section 11.2 above, Genentech shall be automatically granted a nonexclusive, sublicenseable, license in the Territory under Connetics Patent Rights and Connetics Knowhow arising from the efforts made by Connetics and its sublicensees hereunder in the research and development of Licensed Products, to make, have made, use, sell, offer for sale or import Licensed Products and shall be automatically granted a right to use all of Connetics' regulatory submissions made by or on behalf of Connetics for Interferon Gamma and Licensed Products. If Genentech sells a commercial product under the license granted in this Section 11.3 that would, but for the license granted herein, infringe a claim of such Connetics Patent Rights or that is based upon, incorporates or utilizes such Connetics Knowhow, Genentech shall pay Connetics a royalty, under terms and conditions to be mutually agreed upon by the Parties, such royalty to be commensurate with the value contributed by such Connetics Patent Rights and Connetics Knowhow to such commercial product, but in no event shall such royalty

exceed two percent (2%) of Genentech's net sales of such commercial product. As used herein, "net sales" shall have the equivalent definition given to Net Sales in Section 1.25 above.

(b) Upon the effective date of termination by Genentech pursuant to Section 11.2 above, Connetics shall promptly provide Genentech with copies of all related documentation regarding Connetics Patent Rights and Connetics Knowhow arising from the efforts made by Connetics and its sublicensees hereunder in the research, development and manufacture of Licensed Products, whether written or electronic, and materials, including biological materials, in the form existing as of the effective date of such termination, reasonably necessary for Genentech to exercise its license rights under Section 11.3(a) above. Such transfer shall be made in a timely and orderly fashion and in a manner such that the value of what is being transferred is preserved in all material respects. Connetics shall promptly take all appropriate and necessary actions, including action before the involved regulatory agency, to effect transfer to Genentech of, and shall also permit Genentech to reference, any FDA submissions, including, without limitation, any PLA or BLA filed with the FDA with respect to Licensed Products. Within ninety (90) days of such assignment and completion of all such appropriate and necessary actions, Genentech will reimburse Connetics for its actual expenses incurred in preparing documentation for filing or referencing the submission and in taking such appropriate and necessary action related to such transfer or referencing.

11.4 Connetics' Rights on Termination. Should Connetics terminate this Agreement pursuant to Section 11.2 above, Genentech shall grant to Connetics (a) an exclusive, sublicenseable, royalty-bearing license, according to royalty terms described in

Sections 8.3 and 8.4 within the Field of Use in the Territory, under terms and conditions agreed upon by the Parties, under the Genentech Patent Rights and Genentech Knowhow in order to permit Connetics to continue using, selling, offering for sale and importing Licensed Products in the Field of Use in the Territory (excluding, with respect to the fields of scleroderma and infectious disease or condition caused by human papillomavirus, Licensed Products containing any form of Interferon Gamma other than Genentech Gamma Interferon Δ 3, as that term is defined in the Biogen License), (b) a non-exclusive, sublicenseable, royalty-bearing license, (conforming to the license grant in Section 2.1 (b) above) according to royalty terms described in Sections 8.3 and 8.4 in the Territory , under terms and conditions agreed upon by the Parties, under the Genentech Patent Rights and Genentech Knowhow in order to permit Connetics to continue using, selling, offering for sale and importing Licensed Products containing any form of Interferon Gamma other than Genentech Gamma Interferon Δ 3 (as that term is defined in the Biogen License) in the Territory in the fields of scleroderma and infectious disease or condition caused by human papillomavirus, (c) a non-exclusive, sublicenseable license (the royalty for which is already included in clause (a) above) in the Territory in the fields of scleroderma and infectious disease or condition caused by human papillomavirus, under terms and conditions agreed upon by the Parties, under the Biogen License Rights in order to permit Connetics to continue using, selling, offering for sale and importing Licensed Products (except those Licensed Products containing Biogen Gamma Interferon Δ 0) in the field of scleroderma and infectious disease or condition caused by human papillomavirus in the Territory and (d) a non-exclusive sublicenseable license (the royalty for which is already included in clause (a) above) under Genentech Patent Rights and Genentech Manufacturing Knowhow in order to

permit Connetics to continue making and having made Licensed Products in the Field of Use in the Territory.

11.5 Bankruptcy. Either Party may, in addition to any other remedies available to it by law or in equity, terminate this Agreement, in-whole or in part as the terminating Party may determine, by written notice to the other Party in the event the other Party shall have become bankrupt, or shall have made an assignment for the benefit of its creditors or there shall have been appointed a trustee or receiver of the other Party or for all or a substantial part of its property or any case or proceeding shall have been commenced or other action taken by or against the other Party in bankruptcy or seeking reorganization, liquidation, dissolution, winding-up, arrangement, composition or readjustment of its debts or any other relief under any bankruptcy, insolvency, reorganization or other similar act or law of any jurisdiction now or hereafter in effect and any such event shall have continued for sixty (60) days undismissed, unbonded and undischarged. All rights and licenses granted under to this Agreement by one Party to the other Party are, and shall otherwise be deemed to be, for purposes of Section 365 (n) of the Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101 (56) of the Bankruptcy Code. The Parties agree that the licensing Party under this Agreement shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code in the event of a bankruptcy by the other Party. The Parties further agree that in the event of the commencement of a bankruptcy proceeding by or against one Party under the Bankruptcy Code, the other Party shall be entitled to complete access to any such intellectual property pertaining to the rights granted in the licenses hereunder of the Party by or against whom a bankruptcy proceeding has been commenced and all embodiments of such intellectual property.

11.6 Unilateral Termination. In addition to any other right of termination provided herein, Connetics shall have the right to terminate this Agreement for any reason, with or without cause upon six (6) months' prior written notice to Genentech. If Connetics terminates this Agreement pursuant to this Section 11.6, Connetics agrees that for the following three (3) years it will not use, sell or acquire from any third party (whether by license or otherwise) any Licensed Product in the Field of Use. If Connetics terminates this Agreement pursuant to this Section 11.6, the licenses granted hereunder shall terminate and Genentech shall automatically have all of the rights set forth in Sections 11.3(a) and (b) of this Agreement.

11.7 Survival of Certain Provisions. Termination of this Agreement for any reason shall not release either Party from any obligation arising prior to the date of termination. The provisions of Sections 1.0, 2.4 (except in the event of termination of this Agreement by Connetics pursuant to Section 11.2), 11.3(a) and (b) (except in the event of termination of this Agreement by Connetics pursuant to Section 11.2), 11.4 (except in the event of termination of this Agreement by Genentech pursuant to Section 11.2), and Articles 5.0, 7.0, 9.0, 10.0, 11.0 (except as provided in this paragraph) and 12.0 shall survive any termination of this Agreement.

12.0 General Provisions

12.1 Notices. All notices which may be required pursuant to this Agreement: (i) shall be in writing, (ii) shall he addressed, in the case of Genentech (except as otherwise specified herein), to the Corporate Secretary at the address set forth at the beginning of this Agreement, and in the case of Connetics, to the Vice President - Intellectual Property at the

address set forth at the beginning of this Agreement, (or to such other person or address as either Party may so designate from time to time), (iii) shall be mailed, postage-prepaid, by registered mail or certified mail, return receipt requested, or transmitted by courier for hand delivery or transmitted by facsimile and (iv) shall be deemed to have been given on the date of receipt if sent by mail or on the date of delivery if transmitted by courier or facsimile. Notices by facsimile may be sent to the following numbers: for Connetics, to (650) 843-2899; for Genentech, to (650) 952-9881.

12.2 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the state of California (other than its choice of law principles).

12.3 Entire Agreement. This Agreement is the entire agreement between the Parties, and there are no prior written or oral promises or representations not incorporated herein or therein, except that certain Confidentiality Agreement between the Parties dated January 9, 1997 which shall remain in full force and effect. This Agreement shall supersede and replace the Prior Agreement in its entirety, and the Prior Agreement shall be terminated automatically as of the Effective Date. No amendment or modification of the terms of this Agreement shall be binding on either Party unless reduced to writing and signed by an authorized officer of the Party to be bound.

12.4 Binding Effect and Assignment. This Agreement shall be binding upon and inure to the benefit of the Parties hereto and their respective permitted successors and assigns. This Agreement shall not be assignable by either Party without the other's prior written consent, provided however, that either Party may assign this Agreement, without the other Party's written consent but after providing thirty (30) days prior written notice to the other Party, to any successor pursuant to a consolidation or merger of such Party with or into

any other corporation or corporations that results in a change of greater than 50% of the voting control of such Party, or a sale, conveyance or disposition of all or substantially all of the assets of such Party or the effectuation by such Party of a transaction or series of related transactions in which more than 50% of the voting power of such Party is disposed of.

12.5 Waiver. The waiver by a Party hereto of any breach of or default under any of the provisions of this Agreement or the failure of a Party to enforce any of the provisions of this Agreement or to exercise any right thereunder shall not be construed as a waiver of any other breach or default or as a waiver of any such rights or provisions hereunder.

12.6 Severability. If any part of this Agreement shall be invalid or unenforceable under applicable law, such part shall be ineffective only to the extent of such invalidity or unenforceability, without in any way affecting the remaining parts of this Agreement. In addition, the part that is ineffective shall be reformed in a mutually agreeable manner so as to as nearly approximate the intent of the Parties as possible.

12.7 Publicity. Connetics and Genentech agree that, except as may otherwise be required by applicable laws, regulations, rules, or orders, including the disclosure requirements of the Securities and Exchange Commission ("SEC"), no information concerning this Agreement and the transactions contemplated herein (except information which is already in the public domain) shall be made public by either Party without the prior written consent of the other Party. Notwithstanding the foregoing, with respect to complying with the disclosure requirements of the SEC; in connection with any required SEC filing of this Agreement by Connetics, Connetics shall seek confidential treatment of portions of this Agreement from the SEC and Genentech shall have the right to review and comment on such an application for confidential treatment prior to its being filed with the SEC. Genentech

shall provide its comments, if any, on such application as soon as practicable and in no event later than seven (7) days after such application is provided to Genentech. To assist Connetics in its compliance with SEC disclosure obligations, Genentech shall provide to Connetics, within fourteen (14) days of the Effective Date, electronic copies of this Agreement (and all exhibits hereto) and the Supply Agreement. In addition, notwithstanding the foregoing, Connetics shall have the right to disclose information concerning this Agreement and the transactions contemplated herein to its legal representatives, advisors, prospective investors, investors, third party auditors, sublicensees and prospective sublicensees hereunder to the extent reasonably necessary and under obligations of confidentiality no less stringent than those provided for in Article 7.0.

12.8 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original for all purposes, but all of which together shall constitute one and the same instrument.

12.9 Force Majeure. Neither Party shall be liable to the other for its delay or failure to perform under this Agreement or shall have any right to terminate this Agreement for any such delay or failure in performance attributable to any act of God, flood, fire, explosion, strike, lockout, labor dispute, casualty or accident, war, revolution, civil commotion, act of public enemies, blockage or embargo, injunction, law, order, proclamation, regulation, ordinance, demand or requirement of any government or subdivision, authority or representative of any such government, or any other cause beyond the reasonable control of such Party, if the Party affected shall give prompt notice of any such cause to the other Party. The Party giving such notice shall thereupon be excused from such of its obligations, hereunder for the period of time that it is so disabled.

12.10 Headings. Headings are for the convenience of reference only and shall not control the construction or interpretation of any of the provisions of this Agreement.

12.11 No Partnership. Nothing in this Agreement is intended or shall be deemed to constitute a partnership, agency, employer-employee, or joint venture relationship between the Parties.

[Signature page follows]

IN WITNESS WHEREOF, the Parties have caused this Agreement to be duly executed by its duly authorized representatives as of the date set forth above.

GENENTECH, INC.		**CONNECTICS CORPORATION**	
By:	/s/Nicholas J. Simon	By:	/s/Thomas Wiggons
Name:	Nicholas J. Simon	Name:	Thomas Wiggons
Title:	Vice President, Business and Corporate Development	Title:	President/CEO

Exhibit A

Patent Applications and Patents Included in Genentech Patent Rights

U.S. Serial Number	U.S. Patent Number
08/460,524	pending
08/460,539	pending
	5,690,925
	5,582,824
	5,151,265
	5,200,177
	5,112,605
	5,196,191
	5,096,705
	5,574,137
	5,248,499

Exhibit B

[…***…]

Exhibit C

[…***…]

Exhibit D

Third Party Sponsored Studies

[…***…]

Exhibit E

Clinical Development Milestones

[…***…]

Exhibit F

Clinical Reports

The following information/reports will be provided to Genentech in a timely manner:

- FDA Meeting Minutes
- IND(s)
- Initial
- Updates (if applicable)
- Annual Report(s)
- Investigator Brochure(s)
- Clinical Studies:
- Protocol(s)
- Prior to FDA Submission
- First Patient-In (FPI)
- First Patient-Out (FPO)
- Last Patient-In (LPI)
- Last Patient-Out (LPO)
- Serious Adverse Event (SAE) Summary
- Clinical Study Interim Analysis and Update(s) (if applicable)
- Go/Non-Go Decision Minutes
- Clinical Study Final Report(s)
- Draft
- Final Copy

Exhibit G

Third Party Royalties

Royalties are payable under the […***…] License, as follows (capitalized terms shall have the meanings defined in the […***…] License): a […***…] royalty is payable on Net Sales of gamma interferon in Approved Countries in the Territory for the prophylaxis or treatment of atopic dermatitis and/or steroid-dependent asthma, where there is substantial protection from an issued Licensed Patent for the approved indication and where the Licensee has enjoyed Market Exclusivity. The royalty rate is […***…] on Net Sales in the Licensed Field in Approved Countries where the Licensee enjoyed Market Exclusivity but where there is no substantial patent protection, or while the Licensed Patent applications covering the indication are still pending, provided that such applications have been diligently prepared, filed and maintained. The royalty rates described above are reduced by […***…] for Approved Countries where the Licensee has not enjoyed Market Exclusivity.

Exhibit H

TRANSFER DATE ACTIVITIES FOR COMMERCIAL SALES OF ACTIMMUNE FOR CGD

Prior to the Transfer Date, as defined in Section 1.29 of this Agreement, the following activities must be completed by the appropriate Party as described below:

I. Regulatory Requirements

1. FDA License – Connetics must obtain all licenses, including license numbers, required for the sale of Actimmune for CGD by Connetics. Connetics shall also obtain a NDC number.

2. PLA/IND Transfer – Genentech shall transfer to Connetics the PLA and IND for CGD on file with the FDA.

3. Connetics must obtain FDA review and approval, as required by law or regulation, for Connetics' labels, product insert and packaging for sale of Actimmune for CGD.

4. Genentech shall transfer its safety information to Connetics for Actimmune, as provided in Section 2.5(g) of this Agreement. Connetics shall establish a safety database system for Actimmune, such that as of the Transfer Date, Connetics shall be responsible for all safety-related requirements under FDA regulations, including the reporting of adverse events.

5. Prior to the Transfer Date, Connetics shall establish all procedures, controls and other methods and capabilities needed in order to comply with all requirements, laws and regulations applicable to the use, distribution and sale of Actimmune for CGD.

II. Quality Control, Product Testing

1. To the extent that Connetics is required by law or regulation to conduct any quality control, quality assurance and/or stability testing of Actimmune sold for CGD, in addition to any such testing to be conducted by Genentech pursuant to the Supply Agreement, Connetics shall establish procedures and obtain regulatory approval to do so prior to the Transfer Date.

III. Uninsured Patient Program

Connetics shall have established an uninsured patient program, including procedures for determining patient eligibility. Genentech shall transfer to Connetics its existing information regarding such patients prior to the Transfer Date, to the extent it has received consent from such patients to do so. Connetics shall notify Genentech prior to the Transfer Date which of the patients participating in Genentech's uninsured patient program, and for which Genentech has transferred information, shall receive drug under Connetics' uninsured patient program.

IV. Product Distribution and Sale

1 Connetics shall establish product distribution and inventory systems for Actimmune. Genentech will provide to Connetics the name of its current distributor.

2. Connetics shall establish systems and personnel required to address customer inquiries, medical information requests and product returns.

Exhibit 10.65

*****Text Omitted and Filed Separately with the Securities and Exchange Commission. Confidential Treatment Requested Under 17 C.F.R. Sections 200.80(b)(4) and 240.24b-2.**

AMENDMENT NO. THREE
TO
LICENSE AGREEMENT

THIS AMENDMENT NUMBER THREE TO LICENSE AGREEMENT FOR INTERFERON GAMMA ("Amendment") is entered into effective April 27, 1999 (the "Amendment Effective Date"), by and between Genentech, Inc. ("Genentech") and Connetics Corporation ("Connetics"). Genentech and Connetics may each be referred to herein as a "Party" and jointly as the "Parties."

RECITALS

A. The Parties have previously entered into that certain License Agreement for Interferon Gamma, dated May 5, 1998, as amended on December 23, 1998 and on January 15, 1999 (the "License Agreement").

B. Pursuant to Section 2.3(c) of the License Agreement, Connetics has the right to sublicense certain of its rights under the Agreement to InterMune Pharmaceuticals, Inc. ("InterMune"), and has in fact entered into such sublicense to that effect dated August 21, 1998.

C. The Parties have entered into that certain letter agreement dated January 5, 1999 and revised on March 1, 1999 (the "Letter Agreement"), documenting the intent and agreement of Connetics and Genentech with respect to certain additional rights to be granted to Connetics and its sublicensees under the Genentech License, pending the preparation of an amendment to the License Agreement.

D. In consideration of such additional rights, InterMune will issue to Genentech shares of Genentech Series A-1 Preferred InterMune stock on the terms and conditions set forth in that certain stock purchase agreement between Genentech and InterMune of even date herewith.

E. The Parties now desire to enter into a definitive amendment to the License Agreement, as of the Amendment Effective Date, through which Genentech shall grant, and Connetics and InterMune shall accept, such certain additional rights under the License Agreement.

N OW , THEREFORE , in consideration of the foregoing and of the mutual covenants and conditions herein contained, and intending to be legally bound hereby, the Parties mutually agree as follows:

1. Terms not otherwise defined in this Amendment shall have the meanings defined in the License Agreement.

2. A new Section 1.7.1 is hereby added to read in its entirety as follows:

1.7.1 “Combination Product Adjustment” shall mean the following: in the event that a Licensed Product is sold in the form of a combination product containing one or more active ingredients or components in addition to such Licensed Product, Net Sales for such combination product will be adjusted by multiplying actual Net Sales of such combination product by the fraction A/(A + B) where A is the invoice price of the Licensed Product, if sold separately, and B is the invoice price of any other active ingredient(s) or component(s) in the combination, if sold separately. If, on a country-by-country basis, the other active ingredient(s) or component(s) in the combination are not sold separately in said country, Net Sales shall be calculated by multiplying actual Net Sales of such combination product by the fraction A/C where A is the invoice price of the Licensed Product if sold separately, and C is the invoice price of the combination product. If, on a country-by-country basis, neither the Licensed Product nor the other active ingredient(s) or component(s) of the combination product is sold separately in said country, Net Sales allocable to the Licensed Product shall be determined by mutual agreement reached in good faith by the Parties based on an equitable method of determining such Net Sales that, among other considerations, takes into account, on a country-by-country basis, variations in potency, the relative contribution of each active ingredient or component in the combination product and the relative value to the end-user of each active ingredient or component.

3. Section 1.12 of the License Agreement is hereby deleted and replaced in its entirety as follows:

1.12 “Field of Use” shall mean the administration to humans of Licensed Protein Product for the treatment or prevention of any human disease or condition, […***…]. Each “indication” listed on Exhibit E attached hereto shall be referred to herein individually as an “Area of the Field of Use” and collectively as “Areas of the Field of Use.”

4. A new Section 1.15.1 is hereby added to the Agreement to read in its entirety as follows:

1.15.1 “Gene Therapy Field of Use” shall mean the administration to humans of Licensed Gene Product for Gene Therapy for the treatment or prevention of any human disease or condition, […***…].

5. Section 1.18 of the License Agreement is hereby deleted and replaced in its entirety as follows:

1.18 “Genentech Patent Rights” shall mean all patents and patent applications and any patents issuing therefrom, together with any extensions, reissues, reexaminations, substitutions, renewals, divisions, continuations and continuations-in-part thereof:

(a) that are owned or controlled by Genentech presently or hereafter, during the term of this Agreement, and under which Genentech is free to license or sublicense; and

(b) to the extent they claim or directly relate to: (i) Interferon Gamma or the manufacture or use of Interferon Gamma in the Field of Use, or (ii) IG Nucleotide Sequence or the manufacture or use of IG Nucleotide Sequence in the Gene Therapy Field of Use;

including, without limitation, the patent rights granted under that certain license agreement between Genentech and Children's Medical Center Corporation, dated July 16, 1990 (the "CMCC License"), but specifically excluding any rights granted to Genentech under the Biogen License. Genentech Patent Rights shall include, without limitation, the patents and patent applications listed in Exhibit A attached hereto. Notwithstanding the foregoing, Genentech Patent Rights shall exclude any rights Genentech acquires after the Effective Date under third-party license agreements, with the exception of those rights acquired under the CMCC License, unless and until the Parties mutually agree on terms and conditions for the sublicense of such rights from Genentech to Connetics.

6. A new Section 1.20.1 of the License Agreement is hereby added to read in its entirety as follows:

1.20.1 "IG Nucleotide Sequence" shall mean any DNA or RNA sequence encoding Interferon Gamma.

7. Section 1.22 of the License Agreement is hereby deleted and replaced in its entirety as follows:

1.22 "Licensed Product" shall mean, collectively:

(a) Any pharmaceutical formulation containing Interferon Gamma, whether alone or together with or incorporated into any other substance or product or material or device, whether active or not, and which (i) but for the licenses granted hereunder, the manufacture, use, sale, offer for sale or importation of which in the Territory would infringe or contribute to the infringement of the Genentech Patent Rights in the Territory, or (ii) is based upon or incorporates or utilizes Genentech Knowhow (a "Licensed Protein Product"); and

(b) Any pharmaceutical formulation containing the IG Nucleotide Sequence, whether alone or together with or incorporated into any other substance or product or material or device, whether active or not, and which but for the licenses granted hereunder, the manufacture, use, sale, offer for sale or importation of which in the Territory would infringe or contribute to the infringement of the Genentech Patent Rights in the Territory (a "Licensed Gene Product").

8. The following two sentences are hereby added to the end of Section 1.25:

[…***…], shall also be deducted from the gross invoiced sales prices charged for such Licensed Products in determining Net Sales for such Licensed Products. In the event that a Licensed Product is sold in the form of a combination product containing one or more active ingredients or components in addition to such Licensed Product, Net Sales for such combination product will be calculated in accordance with the Combination Product Adjustment."

9. Section 1.28 of the License Agreement is hereby deleted and replaced in its entirely as follows:

1.28 "Territory" shall mean the United States of America, and its territories and possessions, and Japan.

10. A new Section 1.37 is hereby added to the License Agreement to read in its entirety as follows:

1.37 "Third Party Product Rights" shall mean any rights licensed or sublicensed to any third party by Genentech as of the Effective Date to use, manufacture or sell (a) Interferon Gamma, (b) the IG Nucleotide Sequence or (c) any pharmaceutical formulation containing either or both of Interferon Gamma and the IG Nucleotide Sequence, whether alone or together with or incorporated into any other substance or product or material or device, whether active or not; […***…].

11. Section 2.1 of the License Agreement is hereby deleted and replaced in its entirety as follows:

2.1 Patent and Knowhow License Grants.

(a) Genentech hereby grants to Connetics an exclusive license, even as to Genentech, under Genentech Patent Rights and under Genentech Knowhow to use, sell, offer for sale and import (but not to make or have made) Licensed Protein Products in the Field of Use in the Territory (excluding Japan), (excluding, with respect to the fields of (i) scleroderma and (ii) infectious disease or condition caused by human papillomavirus, Licensed Protein Products containing any form of Interferon Gamma other than Genentech Gamma Interferon Δ 3 (as that term is defined in the Biogen License)). Notwithstanding the foregoing, Genentech reserves the right to use (but not to import, offer for sale or sell) Licensed Protein Products within the Field of Use solely for non-commercial research purposes.

(b) Genentech hereby grants to Connetics a non-exclusive license under Genentech Patent Rights and under Genentech Knowhow to use, sell, offer for sale and import (but not to make or have made) Licensed Protein Products containing any form of Interferon Gamma other than Genentech Gamma

Interferon Δ 3 (as that term is defined in the Biogen License) in the Territory (excluding Japan) in the fields of: (i) scleroderma and (ii) infectious disease or condition caused by human papillomavirus.

(c) Genentech hereby grants to Connetics a non-exclusive sublicense under the Biogen License Rights to use, sell, offer for sale and import Licensed Protein Products (excluding Licensed Protein Products containing Biogen Gamma Interferon Δ 0 (as that term is defined in the Biogen License)) in the Territory (excluding Japan) in the fields of scleroderma and infectious disease or condition caused by human papillomavirus.

(d) Genentech hereby grants to Connetics a non-exclusive license under Genentech Patent Rights to make or have made in the Territory (excluding Japan) Licensed Protein Products for use or sale in the Field of Use in the Territory (excluding Japan).

(e) Genentech hereby grants to Connetics a non-exclusive license under Genentech Patent Rights and Genentech Knowhow to use non-human animal species derived homologues of Interferon Gamma ("Non-human Interferon Gamma") solely for non-commercial research purposes to support the Field of Use in the Territory (excluding Japan). Genentech hereby grants to Connetics a non-exclusive license under Genentech Patent Rights to use non-human animal species derived homologues of IG Nucleotide Sequence ("Non-human Interferon Gamma-encoding IG Nucleotide Sequence") solely for non-commercial research purposes to support the Gene Therapy Field of Use in the Territory (excluding Japan).

(f) Genentech hereby grants to Connetics a co-exclusive license under Genentech Patent Rights to use, make, have made, import, offer for sale and sell Licensed Gene Products in the Gene Therapy Field of Use in the Territory (excluding Japan). Notwithstanding the foregoing, Genentech reserves the right to use (but not to import, offer for sale or sell) Licensed Gene Products within the Gene Therapy Field of Use solely for non-commercial research purposes. As used in this subsection (f), "co-exclusive" shall mean that (i) Genentech shall not grant a license to any party other than Connetics to use, make, have made, import, offer for sale or sell Licensed Gene Products in the Gene Therapy Field in the Territory (excluding Japan) […***…], and (ii) Genentech shall not authorize or approve any grant or assignment […***…].

(g) (i) Genentech hereby grants to Connetics an exclusive license, even as to Genentech, under Genentech Patent Rights and under Genentech Knowhow, in Japan to make, have made, use, sell, offer for sale and import […***…]

[…***…].

(ii) Connetics, its Affiliates and sublicensees hereunder shall […***…], to the extent based, in whole or in part, […***…] for indications (including, without limitation, the treatment of […***…]. Connetics' and its Affiliates' and sublicensees' […***…] shall terminate with respect to […***…].

(iii) In the event that any Third Party Product Rights held by a third party […***…] revert to Genentech, then Genentech shall notify Connetics or its designated sublicensee in Japan of such reversion, and upon such notice Genentech shall be deemed to have automatically granted to Connetics the license under Genentech Patent Rights and under Genentech Knowhow to all such reverted rights, which license shall be exclusive to the extent that such reverted rights were exclusive. All rights granted to Connetics pursuant to this subsection (iii) shall be subject to the terms of this Agreement, including without limitation subsection (ii) above, Section 3.2(g) and Section 8.3.

(h) In the event that any Third Party Product Rights (other than those described in subsection (g) above) shall revert to Genentech, then Genentech shall notify Connetics of such reversion. For the ninety (90) day period following its receipt of such notice, Genentech and Connetics shall negotiate exclusively in good faith the reasonable commercial terms upon which Genentech would be willing to grant to Connetics the license to such reverted rights. If the Parties fail to enter a written agreement for a license to such rights by the end of such ninety (90) day period, then Genentech shall have no further obligation to Connetics with respect to such rights; provided that for six (6) months following such ninety

(90) day period, Genentech shall not enter into an agreement to grant a license to such rights with a third party on terms that, taken as a whole, are less favorable to Genentech than those last offered by Connetics for such rights. […***…]. Nothing in the preceding sentence shall imply any […***…]. Connetics may not transfer its rights under this Section 2.1(h) to any party other than InterMune without Genentech's prior written consent.

Except as expressly granted herein, there are no implied licenses under the Genentech Patent Rights or any other intellectual property rights owned or controlled by Genentech.

12. Section 2.3(b) of the License Agreement is hereby deleted and replaced in its entirety as follows:

(b) Connetics may grant one or more sublicenses under the rights granted in Sections 2.1(a), (b), (c), (e), (f) and (g) in the Field of Use and the Gene Therapy Field of Use, on thirty (30) days prior written notice to Genentech, and subject to Genentech's prior written approval, which approval shall not be unreasonably withheld.

13. A new Section 3.2(g) is hereby added to read in its entirely as follows:

(g) In addition to the Clinical Development Milestones (as set forth in Exhibit E hereto), Connetics shall use its Best Efforts to develop and commercialize Licensed Products: (i) in the Field of Use with respect to indications and diseases that, under the provisions of this Amendment, have been added to the "Field of Use" as defined in the original License Agreement executed as of May 5, 1998, and (ii) in the Gene Therapy Field of Use. Such additional indications and diseases in the Field of Use, and the Gene Therapy Field of Use, collectively are referred to in this subsection (g) as the "Additional Indications." In the event that Connetics is not conducting such development efforts with respect to any Additional Indication(s) in a country or countries in the Territory as of the […***…] (or if rights to such Additional Indication were granted to Connetics pursuant to Section 2.1(g)(iii), then as of the […***…] that Genentech notifies Connetics or its designated sublicensee regarding such rights as set forth in that Section) or at any time thereafter, Genentech shall have the right to terminate this Agreement, and the licenses granted hereunder, with respect to Licensed Products for such Additional Indication(s) in such country or countries, upon […***…] days prior written notice to Connetics, unless Connetics can reasonably

demonstrate, during such notice period, by its written records that as of the date of such notice it is conducting such development efforts with respect to such Additional Indication(s) in such country or countries.

14. Sections 8.2(a) and (b) of the License Agreement are hereby deleted and replaced in their entirety as follows:

(a) […***…] within thirty (30) days following the dates on which the first NDA or BLA, as applicable, for a Licensed Protein Product is filed with the FDA by Connetics for […***…]; provided however, that such milestone payments shall only be paid once for each of the foregoing indications, and shall not be paid upon the filing of a NDA or BLA for an osteopetrosis or any mycobacterial infection indication.

(b) […***…] within thirty (30) days following the date Connetics receives the first FDA approval of […***…]; provided however, that such milestone payment shall only be paid once for each of the foregoing indications, and shall not be paid upon receipt of FDA approval for commercial sale for an osteopetrosis or any mycobacterial infection indication.

15. Section 8.3 of the License Agreement is hereby deleted and replaced in its entirety as follows:

8.3 Royalties. Connetics shall pay Genentech the following royalties on Net Sales of Licensed Products by Connetics and its sublicensees:

(a) For annual aggregate Net Sales of all Licensed Protein Products in the Territory (excluding Japan) of up to three million seven hundred thousand dollars ($3,700,000), a royalty rate equal to forty-five percent (45%) of such Net Sales.

(b) In addition to the payment of the royalty rate specified in (a) above, for annual aggregate Net Sales of all Licensed Protein Products in the Territory (excluding Japan) exceeding three million seven hundred thousand dollars ($3,700,000), a royalty rate equal to ten percent (10%) of such Net Sales exceeding $3,700,000.

(c) For Net Sales of all Licensed Protein Products in Japan, a royalty rate equal to […***…] of such Net Sales; *provided, however* , that in the event that […***…] for an indication for which InterMune has exclusive rights under Section 2.1(g), the foregoing royalty rate shall be reduced to […***…] for Net Sales of […***…] in Japan for such indication […***…]

[…***…]. For the sake of clarity, Net Sales of Licensed Protein Products to which Connetics acquires rights pursuant to Section 2.1(g)(iii) shall be subject to this subsection (c).

(d) (i) For Net Sales of Licensed Gene Product in the Territory, where such Licensed Gene Product is used in conjunction with a Licensed Protein Product for the treatment or prevention of a given indication in a given patient population, a royalty rate equal to […***…] of such Net Sales. As used in this subsection (d), "indication" shall mean any particular medical condition within the Field of Use and Gene Therapy Field of Use, including but not limited to labeling claims approved by a regulatory agency.

(ii) For Net Sales of Licensed Gene Product in a country in the Territory, where such Licensed Gene Product is used in a given patient population for the treatment or prevention of the same indication for which a given Licensed Protein Product is used in such patient population, a royalty rate equal to (A) […***…] of such Net Sales during the […***…] period following the first commercial sale of such Licensed Gene Product in such country for the treatment or prevention of such indication in such patient population by Connetics, or its Affiliates and sublicensees (the "First Commercial Sale"); (B) […***…] of such Net Sales during the […***…] period following the First Commercial Sale; and (C) […***…] of such Net Sales beginning on the […***…] anniversary of the First Commercial Sale and thereafter.

(iii) Notwithstanding the provisions of subsections (i) and (ii) above, in the event that annual Net Sales of a Licensed Gene Product for the treatment or prevention of an indication in a patient population in a country in the Territory […***…] for the treatment or prevention of such indication in such patient population in such country, the royalty rate thereafter applicable to Net Sales of such Licensed Gene Product for the treatment or prevention of such indication in such patient population in such country shall be ten percent (10%) of such Net Sales.

(iv) In the event that Connetics or InterMune determines at any point following […***…] that the above royalty rates are having or are likely to have an adverse impact on Connetics' or InterMune's ability to compete effectively in its sales of such Licensed Gene Product, Connetics or InterMune shall so notify Genentech, and the Parties shall in good faith discuss and attempt to reach a reasonable and mutually agreeable resolution to the situation.

(e) (i) The royalties set forth in subsections (a), (b) and (c) above shall be payable, on a country-by-country basis, until the later of: (A) the expiration or revocation of the last remaining issued patent in such country within the Genentech Patent Rights that covers Licensed Protein Products, or (B) […***…] years from the Effective Date of this Agreement. Notwithstanding the

foregoing, upon the expiration of the last to expire issued patent in each country within the Genentech Patent Rights during the term of this Agreement, thereafter each of the royalty rates set forth in (a), (b) and (c) above shall be reduced by […***…] with respect to such country.

(ii) The royalties set forth in subsection (d) above shall be payable, on a country-by-country basis, until the expiration or revocation of the last remaining issued patent in such country within the Genentech Patent Rights that covers Licensed Gene Products.

16. Section 8.4 of the License Agreement is hereby deleted and replaced in its entirety as follows:

8.4 Third-Party Royalties. If Genentech or Connetics is required to pay any third party a royalty due to the manufacture, use, sale, offer for sale or importation of a Licensed Product in the Territory for or by Connetics or its sublicensees, Connetics shall be responsible for the payment of […***…] of such third-party royalty, *provided however* , that Connetics may deduct from the royalties otherwise payable to Genentech under Section 8.3 above, an amount equal to […***…] of such third party royalties incurred only due to use patents in the Field of Use or in the Gene Therapy Field of Use in the Territory, provided that the amount deducted shall not exceed […***…] of the royalties otherwise payable by Connetics to Genentech under Section 8.3. For purposes of clarification, such deductions shall not apply to […***…]. Attached hereto as Exhibit G is a list of all such royalty obligations to third parties known to Genentech as of the Effective Date without diligent search. No later than thirty (30) days from the Effective Date, Genentech shall complete a reasonable internal investigation of its records and update Exhibit G, as necessary, to accurately reflect all such royalty obligations to third parties to the best of Genentech's knowledge; provided however, Connetics acknowledges that Genentech has no obligation to conduct due diligence or any investigation with respect to third party patent rights related to Licensed Products. Genentech shall notify Connetics in writing during the term of this Agreement if it becomes aware of any additional Genentech third party royalty obligations.

17. Section 8.5 of the License Agreement is hereby deleted and replaced in its entirety as follows:

8.5 Royalty Payments.

(a) Royalty payments shall be made to Genentech quarterly within ninety (90) days following the end of each calendar quarter for which royalties are due. Each royalty payment shall be accompanied by a report summarizing the total Net Sales during the relevant three-month period, and the calculation of royalties, if any, due thereon pursuant to Section 8.3.

(b) Notwithstanding subsection (a) above, any royalty payments which accrue during 1999 on Net Sales of Licensed Protein Product sold by Connetics' sublicensee InterMune shall be paid to Genentech in the form of promissory note, in the form attached hereto as Exhibit I. For each calendar quarter in 1999 for which royalty payments are due, InterMune shall execute and deliver to Genentech, within ninety (90) days following the end of each such calendar quarter, a promissory note in the form of Exhibit I, and in the amount of such royalties due to Genentech for such quarter. Each such promissory note shall be accompanied by the report described in Section 8.5(a) above for such quarter. In the event that any such note is delivered by InterMune after such 90 day period, nevertheless interest shall accrue on the date that such note was due.

18. The following provision is hereby inserted as Section 10.4 to the License Agreement:

10.4 Insurance. At all times during the term of this Agreement, Connetics and its sublicensees shall provide the following insurance at its sole cost and expense:

(a) Commercial General Liability, including coverage for products and completed operations (maintained for a period of at least […***…] after the expiration or termination of this Agreement) [...***...]. The policy shall have a limit of no less than […***…] dollars.

(b) Foreign Local Coverages: Where required by law, Connetics and its sublicensees will purchase foreign local coverages in an amount that, at a minimum, satisfies the legal requirements of that jurisdiction.

(c) Policy Conditions: All policies under (a) and (b) above shall:

(i) be written by insurance companies with an A.M. Best's rating of A:VIII or higher (or if Connetics' or its sublicensees policies are not subject to the Best rating, then by carriers who are acceptable to Genentech); and

(ii) add Genentech as an additional insured.

(d) Additionally, Connetics shall use its Best Efforts to obtain from its insurance carrier for the policies described in subsections (a) and (b) covenants:

(i) […***…]; and

(ii) […***…].

Connetics and its sublicensees shall provide Genentech a certificate of insurance which shall reflect the above coverages and provisions, with annual renewals as long as the contract continues.

19. Section 11.1 of the License Agreement is hereby deleted and replaced in its entirety as follows:

11.1 Term. This Agreement shall commence on the Effective Date of this Agreement and, unless terminated earlier, shall expire:

(a) With respect to Licensed Protein Products, at the later to occur of (i) the expiration of the last to expire of any Genentech Patent Rights covering a Licensed Protein Product, or (ii) twenty (20) years from the Effective Date of this Agreement; and

(b) With respect to Licensed Gene Products, at the expiration of the last to expire of any Genentech Patent Rights covering a Licensed Gene Product;

provided, however , that in the event that either the CMCC License or the Biogen License is terminated, the licenses granted by Genentech to Connetics under the CMCC License or the Biogen License shall also terminate. Genentech shall use its Best Efforts to keep the CMCC License and the Biogen License in effect during the term of this Agreement, […***…]. One (1) year before the expiration of this Agreement under Section 11.1(a), the Parties agree to meet and to discuss in good faith extending the term of this Agreement with respect to Licensed Protein Products on terms mutually agreeable to the Parties.

20. Exhibit E of the License Agreement is hereby deleted and replaced in its entirety with new Exhibit E attached hereto and incorporated herein.

21. In consideration for the rights granted to Connetics and its sublicensees under this Amendment, InterMune shall issue to Genentech eight hundred seventy five thousand (875,000) shares of Series A-1 Preferred Stock simultaneously herewith.

22. This Amendment supersedes the Letter Agreement in its entirety. All other terms and provisions of the License Agreement, including all exhibits to that Agreement, will continue in full force and effect as though fully set forth in this Amendment. Nothing in this Amendment shall be construed as affecting Connetics' obligations to be liable and responsible for the performance of all of the obligations of Connetics and its sublicensees under the License Agreement.

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*****Confidential Treatment Requested**

IN WITNESS WHEREOF, the Parties have caused this Amendment to be executed by the respective duly authorized officers as of the date first written above.

GENENTECH, INC.

By: /s/ Nicholas J. Simon

Printed Name: Nicholas J. Simon

Title: Vice President, Business and Corporate Development

CONNETICS CORPORATION

By: /s/ Thomas G. Wiggans

Printed Name: Thomas G. Wiggans

Title: President and Chief Executive Officer

Acknowledged and agreed as to InterMune's rights and obligations hereunder as Connetics' sublicensee under the License Agreement:

INTERMUNE PHARMACEUTICALS, INC.

By: /s/ Scott Harkonen

Printed Name: Scott Harkonen, M.D.

Title: President

Exhibit E

[…***…]

***Confidential Treatment Requested

Exhibit 31.3

Certification of Principal Executive Officer

I, Timothy P. Walbert, certify that:

1. I have reviewed this Amendment No. 3 to the annual report on Form 10-K/A of Horizon Pharma plc; and
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.

Date: May 26, 2017

/s/ Timothy P. Walbert

Timothy P. Walbert
Chairman, President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.4

Certification of Principal Financial Officer

I, Paul W. Hoelscher, certify that:

1. I have reviewed this Amendment No. 3 to the annual report on Form 10-K/A of Horizon Pharma plc; and
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.

Date: May 26, 2017

/s/ Paul W. Hoelscher

Paul W. Hoelscher
Executive Vice President, Chief Financial Officer
(Principal Financial Officer)