18-02908-E

Debra Smetana
ktMINE
940 West Adams
Suite 100
Chicago, IL 60607

U.S. Securities & Exchange Commission
Office of FOIA and Privacy Act Operations
100 F Street, NE
Mail Stop 2465
Washington, DC 20549-5100

Dear Sir or Madam:

Under the Freedom of Information Act (FOIA), please send the confidential portions (i.e. unredacted documents) corresponding to the expiration of the Confidential Treatment Order submitted under Rule 24b-2 of the following company

Exhibit 10.45 to the 12/31/04 10-K, filed by ZymoGenetics, Inc. on 3/14/2005

We authorize $0 for search and review fees, as these documents have been previously requested. Please contact me if search will require additional fees beyond the above mentioned. My daytime phone number is (312) 667-0267

Sincerely,

Debra Smetana

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

March 27, 2018

Ms. Debra Smetana
ktMine
940 West Adams, Suite 100
Chicago, IL 60607

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-02908-E

Dear Ms. Smetana:

This letter is in response to your request, dated and received in this Office on March 1, 2018, for Exhibit 10.45 to the Form 10-K, filed by ZymoGenetics, Inc. on March 14, 2005.

The search for responsive records has resulted in the retrieval of 37 pages of records that may be responsive to your request. They are being provided to you with this letter.

No fees have been assessed for the processing of this request. If you have any questions, please contact me directly at andersonc@sec.gov or (202) 551-8315. You may also contact me at foiapa@sec.gov or (202) 551-7900. You also have the right to seek assistance from Ray J. McInerney as a FOIA Public Liaison or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

Clarissa Anderson

Clarissa Anderson
FOIA Research Specialist

Enclosure

10.45

License Agreement for
Recombinant Factor XIII

This Agreement, effective as of October 4, 2004 (the "**Effective Date**"), is entered into by and among ZymoGenetics, Inc., a Washington corporation whose address is 1201 Eastlake Ave. East, Seattle, WA 98102 ("**ZGEN**"), Novo Nordisk A/S, a Danish corporation whose address is Novo Allé, DK-2880, Bagsvaerd, Denmark ("**Novo**"), and Novo Nordisk Health Care AG, a Swiss corporation and wholly-owned affiliate of Novo whose address is Andreasstrasse 15, 8050 Zürich, Switzerland ("**NN**"). ZGEN and NN are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties.**"

WHEREAS, ZGEN owns and/or controls certain intellectual property rights, regulatory filings, contracts, clinical supplies, biological materials, reagents, assays, protocols, SOPs and know-how with respect to Recombinant Factor XIII and related preclinical and clinical studies;

WHEREAS, NN is a company engaged in the research, development, manufacturing and commercialization of pharmaceutical and biotechnology products;

WHEREAS, NN desires to obtain from ZGEN, and ZGEN desires to grant to NN, rights to such intellectual property, regulatory filings, contracts, clinical supplies, biological materials, reagents, assays, protocols, SOPs and know-how, upon the terms and conditions set forth herein; and

WHEREAS, Novo from time to time carries out certain research and development activities for NN;

NOW, THEREFORE, the Parties and Novo, in consideration of the mutual representations, warranties and covenants contained herein and for other good and valuable consideration, hereby agree as follows:

Article 1
Definitions

Section 1.1. "**Affiliate**" means, with respect to a Party, any other business entity which directly or indirectly controls, is controlled by or is under common control with the Party. The direct or indirect ownership of at least fifty percent (50%) or, if smaller, the maximum allowed by applicable law, of the voting securities of a business entity or of an interest in the assets, profits or earnings of a business entity shall be deemed to constitute control of the business entity. For the avoidance of doubt, ZGEN and NN are not Affiliates of each other.

Section 1.2. "**Agreement**" means this License Agreement for Recombinant Factor XIII, as amended in accordance with its terms.

Section 1.3 "**Avecia**" means Avecia Limited.

Section 1.4 "**Avecia Agreement**" means the agreement between ZGEN and Avecia for the manufacture of rFXIII dated August 15, 2001, as amended by First, Second, Third, Fourth and Fifth Amendments and Programme Amendment Orders, including PAO 4.2 dated March 2001 relating to 3,000 liter fermentation with full processing of an approximate 300-liter aliquot. ★

Section 1.5. "**Aventis Agreement**" means the Exclusive Patent License Agreement between Aventis Behring GmbH (now known as ZLB Holding GmbH, "**Aventis**") and ZGEN dated December 18, 2002, as amended by a First Amendment dated December 8, 2003 and a Second Amendment dated October 1, 2004.

Section 1.6. "**Best of its Knowledge**" means to the best knowledge of senior management or the legal department of ZGEN or NN, as the case may be.

Section 1.7. "**Biologically Active Substance**" means a pharmaceutically active substance that has intrinsic biological or cell stimulatory activity, but not including a substance that acts as a stabilizing agent, excipient or adjuvant or whose primary function is to act as a delivery vehicle.

Section 1.8. "**Calendar Quarter**" means each three (3) month period commencing on January 1, April 1, July 1, or October 1.

Section 1.9. "**Calendar Year**" means each twelve (12) month period commencing on January 1.

Section 1.10. "**Cancer Treatment Indication**" means bleeding in a patient with malignancy that occurs either as a consequence of the malignancy or the treatment of the malignancy and requires medical intervention.

Section 1.11. "**Cardiac Surgery Indication**" means bleeding or oozing of blood in a patient undergoing cardiac surgery or having undergone cardiac surgery that occurs during or following the surgery and requires medical intervention.

Section 1.12. "**Clinical Proof of Concept**" and "**CPOC**" mean demonstration in a Phase II Clinical Trial that the safety and efficacy of the product being tested as compared to placebo meet prospectively defined study endpoints.

Section 1.13. "**Clinical Proof of Concept Study**" and "**CPOC Study**" mean a Phase II Clinical Trial in which the safety and efficacy of the product being tested are compared to placebo using prospectively defined study endpoints.

Section 1.14. "**CMC**" means processes and information typically known as "chemistry, manufacturing and controls" information to be provided to Regulatory Agencies.

Section 1.15. "**Combination Product**" means a Licensed Product that includes one or more Biologically Active Substance(s) other than Recombinant Factor XIII.

Section 1.16. "**Combination rFVIIa/rFXIII**" means a Combination Product that includes both rFXIII and rFVIIa and no other Biologically Active Substances.

Section 1.17. "**Confidential Information**" means all proprietary information and materials, patentable or otherwise, of a Party or Novo disclosed by or on behalf of such disclosing Party or Novo to the receiving Party or Novo, such as, but not limited to, DNA sequences, amino acid sequences, vectors, cells, substances, formulations, techniques, methodology, equipment, data, reports, know-how, assay results, preclinical studies and clinical trials and the results thereof, patent positioning and business plans, including any negative developments.

Section 1.18. "**Congenital Factor XIII Deficiency**" means the lack of adequate factor XIII activity in a patient from birth.

Section 1.19. "**Control**" means the ability to grant licenses or sublicenses without violating the terms of any agreement or other arrangement with any Third Party.

Section 1.20. "**Data Monitoring Committee**" means a committee described in an FDA draft guidance document dated November 2001 and entitled "On the Establishment and Operation of Clinical Trial Data Monitoring Committees" that is established for the purpose of reviewing data from a clinical study, including safety data.

Section 1.21. "**Decision to Submit Registration File**" means notification by NN to ZGEN of the determination by NN's executive management that the clinical and safety data for a given indication are sufficient

for purposes of submitting a Marketing Application for Marketing Approval. Such notification shall be given by NN to ZGEN no later than, and shall be deemed to have been given on (if such notification has not been given), the seventh (7^{th}) day following such management determination.

Section 1.22. "**Dose Escalation**" means sequentially administering increasing doses of an investigational drug or biologic to different cohorts of study subjects until a prespecified event occurs or the maximum desired dose is reached.

Section 1.23. "**Effective Date**" means the date written in the first paragraph of this Agreement.

Section 1.24. "**EMEA**" means the European Agency for the Evaluation of Medicinal Products or the European Commission.

Section 1.25. "**Event Milestone**" has the meaning set forth in **Section 4.2**.

Section 1.26. "**Exhibit**" means an exhibit explicitly referenced as such in this Agreement. All such Exhibits are by such references incorporated into this Agreement as if fully set forth herein.

Section 1.27. "**Factor XIII Product**" means a Licensed Product containing Recombinant Factor XIII as the only Biologically Active Substance.

Section 1.28. "**FDA**" means the United States Food and Drug Administration or any successor agency vested with administrative and regulatory authority to approve testing and marketing of human pharmaceutical or biological therapeutic or diagnostic products in the United States.

Section 1.29 "**FTE**" means the full-time equivalent of a person being employed for one year (including applicable vacations and holidays).

Section 1.30. "**First Commercial Sale**" means, in a country, the first sale by NN or its Affiliate or Sublicensee of the Licensed Product to a Third Party after Marketing Approval to sell the Licensed Product in the country has been granted.

Section 1.31. "**First Patient First Visit**" and "**FPFV**" mean the first visit at which data (e.g., medical history) is collected from the first study subject to determine eligibility to participate in a given clinical study.

Section 1.31A. "**GMP Manufacturing Run**" has the meaning set forth in **Section 5.5(d)**.

Section 1.32. "**Know-How Product**" means a product that (a) contains Recombinant Factor XIII, (b) was developed through use of any Licensed Know-How or otherwise incorporates or embodies any Licensed Know-How, and (c) is not a Patent Product.

Section 1.33. "**Licensed Know-How**" means all inventions, discoveries, know-how, methodologies, technology, tangible materials (including nucleic acids, peptides, vectors, proteins, and the like) that (a) pertain to Recombinant Factor XIII, (b) were invented, discovered, developed or otherwise generated by or for ZGEN, and (c) are owned and Controlled by ZGEN as of the Effective Date. For the avoidance of doubt, Licensed Know-How shall not include such items which: (i) at the time of disclosure is in the public domain; (ii) prior to the disclosure from ZGEN to NN, was in NN's possession; or (iii) are developed independently by NN without any use of any confidential ZGEN know-how or confidential ZGEN patent rights whatsoever. The Technology Transfer Letter lists the information and tangible biological materials, reagents, assays and other items to be transferred to NN pursuant to **Article 5** that contain Licensed Know-How.

Section 1.34. "**Licensed Patents**" means all patents and patent applications, except those identified in a letter to NN from ZGEN dated October 4, 2004 and related divisionals, continuations (in whole or in part),

foreign counterparts, reissues, reexaminations, renewals and extensions thereof and patents issuing thereon, claiming the benefit of a priority date on or before the Effective Date and owned by ZGEN at any time during the term of this Agreement that contain one or more claims specifically naming rFXIII and claiming (i) rFXIII as a composition of matter; (ii) a process, formulation and/or mixture comprising rFXIII, (iii) a method of making or manufacturing rFXIII, or (iv) a method of using rFXIII, and including without limitation:

(a) the patents and patent applications identified in **Exhibit A** and **Exhibit B** attached to this Agreement;

(b) all divisional or continuation, in whole or in part, applications based on any of the foregoing;

(c) any and all foreign applications corresponding to the patent applications described in paragraphs (a) and (b) above;

(d) any and all issued and unexpired patents resulting from any of the applications described in paragraph (a), (b) or (c) above; and

(e) any and all issued and unexpired reissues, reexaminations, renewals or extensions that may be based on any of the patents described in paragraph (a) or (d) above.

Section 1.35. "**Licensed Product**" means either a Know-How Product or a Patent Product.

Section 1.36. "**Marketing Application**" means a Biologics License Application, New Drug Application or an application for any other approval from a Regulatory Agency to market a Licensed Product.

Section 1.37. "**Marketing Approval**" means receipt of written approval from a Regulatory Agency to market and sell a Licensed Product.

Section 1.38. "**Net Sales**" means the gross amount invoiced by NN, its Affiliates and Sublicensees from sales or other dispositions of Licensed Products to any Third Party, less the following with respect to the invoiced Licensed Product:

(a) any direct or indirect credits and allowances or adjustments, including, without limitation, credits and allowances on account of retroactive price adjustments or on account of rejection, recall or return of Licensed Products previously invoiced;

(b) any trade and cash discounts, price reductions or rebates, retroactive or otherwise, imposed by government authorities and fees charged by third party distributors for stocking or maintaining inventories of Licensed Product;

(c) any sales, excise, turnover, value added, or similar taxes and any duties and other governmental charges imposed upon the production, importation, use or sale of Licensed Product(s) and included in the invoiced amount;

(d) applicable transportation, importation, insurance and other handling charges; and

(e) the per unit cost of special delivery devices (including any per unit cost of assembling such special devices) that are included in the invoiced amount and are used for administration of Licensed Product. Such special devices shall not include conventional devices (e.g., tablets, standard syringes, suppositories and/or standard transdermal patches).

No royalty shall be payable on any sale between NN, its Affiliate and/or a Sublicensee unless the purchaser is the end user of the Licensed Product.

Any Licensed Product sold or otherwise disposed of in other than an arm's-length transaction or for other than property (e.g., barter) shall be deemed invoiced at its fair market value in the country of sale or disposition.

Section 1.39. "**Patent Claim**" means a claim of any patent or pending patent application (except a patent application that has been pending for more than seven and one half (7½) years after the initial filing of such patent application in the applicable jurisdiction) within the Licensed Patents or Sublicensed Patents that has not:

(a) lapsed, been disclaimed, withdrawn, canceled, abandoned or admitted to be invalid or unenforceable;

(b) been finally rejected or held invalid by a final decision of a patent-granting or appellate authority from which no appeal has been or can be taken; or

(c) been held invalid or unenforceable in an unappealable decision of a court or competent body having jurisdiction (including a decision which was appealable, but which was not timely appealed).

Section 1.40. "**Patent Product**" means a product that contains Recombinant Factor XIII, the making, using, importation, exportation, offer for sale or sale of which product would infringe, in the absence of the licenses granted under this Agreement, any unexpired Patent Claim.

Section 1.41. "**Phase I Clinical Trials**" means human clinical trials intended to obtain initial data regarding the safety of a Licensed Product.

Section 1.42. "**Phase II Clinical Trials**" means human clinical trials intended to study the safety, dose range and efficacy of a Licensed Product that do not constitute Phase III Clinical Trials of such Licensed Product.

Section 1.43. "**Phase III Clinical Trials**" means human clinical trials that are intended to demonstrate the statistical efficacy and safety of a Licensed Product and that are intended to be the final stage of clinical testing prior to and in support of the filing of a Marketing Application.

Section 1.44. "**Phase III Development Candidate**" means the product to be advanced into Phase III Clinical Trials pursuant to **Section 3.6**.

Section 1.45. "**Primary Endpoint**" means the variable capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of a clinical trial.

Section 1.46. "**Recombinant Factor VIIa**" and "**rFVIIa**" mean a protein that has an amino acid sequence of human factor VIIa or its subunits and that is produced by recombinant DNA techniques (including without limitation, production in prokaryotic and eukaryotic host cells and transgenic animals), including variants, derivatives, modifications, fragments, hybrids, mutants, conjugates, fusion proteins and analogs of such protein. For purposes of **Sections 3.3** through **3.6**, Recombinant Factor VIIa and rFVIIa shall mean the active Factor VIIa protein in NN's product known as NovoSeven®.

Section 1.47. "**Recombinant Factor XIII**" and "**rFXIII**" mean a protein that has an amino acid sequence of human factor XIII or its subunits ($[A_2]$, [B], $[A_2B_2]$ or any combination thereof) and that is produced by recombinant DNA techniques (including, without limitation, production in prokaryotic and eukaryotic host cells and transgenic animals), including variants, derivatives, modifications, fragments, hybrids, mutants, conjugates, fusion proteins and analogs of such protein.

Section 1.48. "**Regulatory Agency**" means:

(a) the FDA;

(b) the EMEA; or

(c) any regulatory body with similar regulatory authority in any other jurisdiction anywhere in the world.

Section 1.49. "**Regulatory Event**" means an adverse event in the regulatory process with a Regulatory Agency with respect to a Licensed Product or an rFVII product that is unexpected and not customary for products of a similar profile. For the avoidance of doubt, a "clinical hold" imposed on a human clinical trial by a Regulatory Agency is a "**Regulatory Event**."

Section 1.50. "**rFXIII Supplies**" has the meaning set forth in **Section 5.4**.

Section 1.51. "**Signature Fee**" has the meaning set forth in **Section 4.1**.

Section 1.52. "**Statistical Analysis**" means the analysis of the Clinical Proof of Concept Study results performed in accordance with **Section 3.5**.

Section 1.53. "**Sublicensed Patents**" means all patents and patent applications licensed to ZGEN pursuant to the UW Agreement and Aventis Agreement, including without limitation

(a) the patents and patent applications identified in **Exhibits C**, **D** and **E** attached to this Agreement;

(b) to the extent licensed to ZGEN, all divisional or continuation, in whole or in part, applications based on any of the foregoing;

(c) to the extent licensed to ZGEN, any and all foreign applications corresponding to the patent applications described in (a) and (b) above;

(d) to the extent licensed to ZGEN, any and all issued and unexpired patents resulting from any of the applications described in paragraph (a), (b) or (c) above; and

(e) to the extent licensed to ZGEN, any and all issued and unexpired reissues, reexaminations, renewals or extensions that may be based on any of the patents described in paragraph (a) or (d) above.

Section 1.54. "**Sublicensee**" means a Third Party to whom NN has granted a license or sublicense under its rights under this Agreement to research, develop, make, have made, use, import, have sold, sell or offer to sell a Licensed Product in one or more countries of the world. For the purpose of any compensation payable to ZGEN hereunder, "**Sublicensee**" shall include a Third Party to whom NN, its Affiliate or another Sublicensee (a) shall have sold or transferred a Licensed Product in bulk (e.g., as bulk rFXIII) or other form and the Licensed Product is changed into another form or composition (e.g., formulation, dose form, etc.) for sale for therapeutic, prophylactic or diagnostic purposes, *provided*, that in the case of a diagnostic Licensed Product, rFXIII acts therein as an active ingredient (through binding or otherwise), or (b) shall have granted the right to distribute one or more Licensed Product(s), wherein such a distributor pays to NN, its Affiliate or such other Sublicensee a royalty based on the revenues received or profits earned by the distributor for the sale of such Licensed Product(s), but shall not include any Third Party where NN, its Affiliate or another Sublicensee merely sells such Licensed Product at a fixed transfer price to such distributor for resale by such distributor and the party is not compensated based on the resale price or profit of such Licensed Product by such distributor.

Section 1.55. "**Technology Transfer Date**" means, with respect to the transfer pursuant to **Section 5.1** of each item of information or physical material described in the Technology Transfer Letter, the date that is a certain number of days after the "Target Date" for such item set forth in Technology Transfer Letter, which "Target Date" is specified as a number of days after execution of this Agreement by the Parties. With respect to those items in the Technology Transfer Letter that have a "Target Date" designated as "closing," the Technology Transfer Date shall be ten (10) days after the execution of this Agreement by the Parties. With respect to those items in the Technology Transfer Letter that have a "Target Date" specified as a number of days, the Technology Transfer Date shall be such number of days plus fifteen (15) days after the execution of this Agreement by the Parties.

Section 1.56. "**Technology Transfer Letter**" means the letter dated October 4, 2004 from ZGEN to NN (with attachments) which lists the information and tangible biological materials, reagents, assays and other items to be transferred to NN by ZGEN.

Section 1.57. "**Third Party**" means any person or entity other than ZGEN, NN, Novo or their respective Affiliates.

Section 1.58. "**Time Milestone**" has the meaning set forth in **Section 4.2**.

Section 1.59. "**UW**" means the University of Washington.

Section 1.60. "**UW Agreement**" means the License Agreement between UW and ZGEN dated February 23, 1989.

Section 1.61. "**WRF**" means Washington Research Foundation.

Section 1.62. "**WRF Agreement**" means the Field-Of-Use Non-Exclusive License Agreement between WRF and ZGEN for Factor XIII effective as of January 7, 2002.

Section 1.63. "**WRF Option**" means the transferable option to obtain a non-exclusive license from WRF described in **Section 3.4** of the WRF Agreement.

Section 1.64. "**ZGEN CD Protocol**" means the ZGEN design of the protocol as summarized in ZGEN's protocol synopses 112C09, 112C11, 112C12 and 112C13 that were submitted to the FDA on March 12, 2004 as part of the EOP2 briefing packet and discussed in a teleconference between ZGEN and the FDA held on June 1, 2004 (the substance of which is summarized in a ZGEN memo dated June 9, 2004).

Section 1.65. "**ZGEN IP**" means the Licensed Patents and Licensed Know-How.

Article 2
License and Rights

Section 2.1. **Grant of License.** Subject to the terms and conditions of this Agreement, ZGEN hereby grants to NN a worldwide, exclusive (even as to ZGEN) license under the ZGEN IP to research, develop, make, have made, use, import, have sold, sell and offer to sell Licensed Products.

Section 2.2. **Grant of Sublicense.** Subject to the terms and conditions of this Agreement, the UW Agreement and the Aventis Agreement, ZGEN hereby grants to NN a worldwide, exclusive (even as to ZGEN) sublicense of its license rights under the UW Agreement and Aventis Agreement to the Sublicensed Patents to research, develop, make, have made, use, import, have sold, sell and offer to sell Licensed Products. Except for the payments to UW by ZGEN pursuant to **Section 4.4**, NN shall comply with and perform in accordance with the terms of the UW Agreement and Aventis Agreement.

Section 2.3. **Sublicenses.** NN may sublicense its rights granted to it pursuant to **Sections 2.1** and **2.2** to one or more Sublicensees. Each sublicense shall be terminable at ZGEN's option upon termination of this Agreement. Each sublicense shall be in writing, shall be subject to and consistent with the terms of this Agreement, and shall contain provisions substantially identical to **Sections 3.1, 4.11, 7.3, 8.7, 9.5, 9.6, 9.8, 9.9, 13.7, 13.8, 13.11, 13.12, 13.15** and **13.17** and **Articles 10** and **12**. NN shall within ten (10) days inform ZGEN of the execution, scope, territory, amendment of scope/territory and termination of each sublicense and the name and address of each Sublicensee. For the avoidance of doubt and notwithstanding the sublicensing of its rights and obligations hereunder, NN shall remain responsible for the full and complete performance of all of NN's obligations and duties under this Agreement, including the making of the payments due under **Article 4**.

Section 2.4. **WRF Agreement.** Subject to the terms and conditions of this Agreement and the WRF Agreement, ZGEN hereby transfers the WRF Option to NN. Within ten (10) days of the execution of this Agreement, ZGEN shall notify WRF of its selection of NN as the transferee of the WRF Option. NN shall be responsible for exercising the WRF Option and for complying with the terms of any license agreement between NN and WRF resulting from the exercise of such option, including the payment of any amounts due to WRF under any such license agreement.

Section 2.5. **Service Contracts.** ZGEN shall cooperate with NN in NN's efforts to establish service contracts, including consulting arrangements, with the parties with whom ZGEN has active, ongoing contracts for providing services to ZGEN in connection with its rFXIII program and shall continue its service contracts identified in **Exhibit F** attached to this Agreement for the benefit of NN for at least three (3) months (or such shorter time as requested by NN and permitted by such agreements), for which it shall receive full reimbursement for its costs thereunder that are incurred after the Effective Date (including any prepaid costs for services during such period).

Section 2.6. **Transfer of Regulatory Filings.** Within ten (10) business days of the execution of this Agreement by the Parties, ZGEN shall file documents with the applicable Regulatory Agencies for the purpose of transferring to NN the regulatory filings, approvals and orphan drug designations listed in **Exhibit G** attached to this Agreement.

Section 2.7. **Avecia Supply Agreement.** Promptly following execution of this Agreement by the Parties, ZGEN shall request that Avecia enter into an agreement with NN on terms and conditions no less favorable than the Avecia Agreement; *provided, however*, that NN shall have the sole responsibility for negotiating the terms and conditions of such agreement directly with Avecia.

Section 2.8. **Government Rights.** NN acknowledges that the Sublicensed Patents identified in **Exhibit C** may be subject to the rights, obligations and limitations of 35 U.S.C. § 200 *et seq.*, and applicable implementing regulations.

Section 2.9. **No Further Rights.** Except as explicitly provided in this **Article 2** and this Agreement, no further or different license or right, express or implied, is granted by ZGEN. NN shall not use, and shall not allow its Affiliates and Sublicensees to use, the ZGEN IP or the Sublicensed Patents for any purpose other than as expressly licensed in this **Article 2** and this Agreement.

Section 2.10. **UW/Aventis Agreements.** ZGEN shall perform its obligations under the UW Agreement and Aventis Agreement, subject to performance by NN of its obligations related thereto (including payment of royalties and milestones under the Aventis Agreement) and hereunder. ZGEN shall provide prompt notice to NN of (a) any notice it receives of alleged breaches of either agreement or (b) to the Best of its Knowledge, any event that constitutes a material breach of either agreement. NN shall provide prompt notice to ZGEN of (a) any notice it receives from Aventis regarding alleged breaches of the Aventis Agreement or (b) to the Best of its Knowledge, any event that constitutes a material breach of the Aventis Agreement. ZGEN shall

not amend, modify or terminate the UW Agreement or the Aventis Agreement without the prior written consent of NN, which consent shall not be unreasonably withheld or delayed.

Article 3
NN's Diligence and Development

Section 3.1. **General Responsibilities of NN.** NN shall, at its sole expense, be solely responsible for the development and commercialization of Licensed Products. NN shall use commercially reasonable efforts that are consistent with its activities (and the activities of its Affiliates, including Novo) with respect to products of similar profit potential and product profile to develop and commercialize Licensed Products under this Agreement. NN, at its sole discretion, may decide on a development plan for any Licensed Product, so long as such development plan complies with the terms and conditions of this **Article 3**, as may be revised by NN to reflect any advice or guidance received from a Regulatory Agency as documented in meeting minutes or correspondence with the Regulatory Agency. All costs related to the development of Licensed Products incurred by NN or ZGEN following execution of this Agreement by the Parties shall be borne by NN, *provided that* any services provided by ZGEN and the costs associated therewith shall have been approved in writing by NN in advance or the reimbursement or payment of ZGEN's costs by NN have been specified in this Agreement (e.g., **Section 2.5** and **Article 5**).

Section 3.2. **Product Development and Commercialization Requirements.**

(a) Subject to **Sections 3.2(b)** and **3.2(c)**, NN shall develop and seek Marketing Approval in the European Union from the EMEA and in the United States from the FDA for a Factor XIII Product for the treatment of Congenital Factor XIII Deficiency. Despite such development and Marketing Approval, NN shall not be required to market a Factor XIII Product for the treatment of Congenital Factor XIII Deficiency.

(b) Notwithstanding **Section 3.2(a)**, NN shall only be required to develop and seek Marketing Approval for a Factor XIII Product for the treatment of Congenital Factor XIII Deficiency (i) in the European Union if both the FDA and EMEA accept the ZGEN CD Protocol (or a protocol of similar magnitude and feasibility which allows the start of a Phase III Clinical Trial directly after a Phase I Clinical Trial) and (ii) in the United States if the FDA accepts the ZGEN CD Protocol (or a protocol of similar magnitude and feasibility which allows the start of a Phase III trial directly after a Phase I Clinical Trial).

(c) Subject to **Section 3.2(e)** and **Section 3.6(c)** or **(d)**, NN shall develop, seek Marketing Approval for and commercialize one or more Licensed Products (or a rFVIIa product in the case of **Section 3.6(e)**) for the treatment of the Cancer Treatment Indication and the Cardiac Surgery Indication in the European Union and United States.

(d) NN, at its sole discretion, may develop, seek Marketing Approval and commercialize Licensed Products for any additional therapeutic indications.

(e) NN shall have the right to terminate the development of a Licensed Product, or the development of an rFVIIa product pursuant to **Section 3.6(e)**, for the treatment of Congenital Factor XIII Deficiency, the Cancer Treatment Indication or the Cardiac Surgery Indication under this **Section 3.2** at any stage of development in the event of an adverse occurrence or condition with respect to CMC, efficacy, safety and/or toxicology related to the Licensed Product or the rFVIIa product, as the case may be, which materially affects NN's ability to progress the therapeutic indication and which cannot be overcome by commercially reasonable efforts. As soon as reasonably practicable after any such occurrence or condition that could reasonably be expected to be grounds for termination under this **Section 3.2(e)**, NN shall notify ZGEN of such occurrence or condition and shall provide ZGEN with information (to the extent available at the time) regarding the situation, including NN's preliminary assessment and NN's estimated time to complete a full assessment. After further investigation and evaluation, and prior to exercising its right to terminate under this **Section 3.2(e)**, NN shall

provide and discuss with ZGEN all relevant information and NN's evaluation regarding (i) the impact of such occurrence or condition on NN's ability to progress the therapeutic indication and (ii) NN's efforts to overcome such occurrence or condition.

Section 3.3. **Dose Escalation Study Requirement.** Subject to **Section 3.2(e)**, NN shall conduct Dose Escalation studies in Phase II Clinical Trials for both the Cancer Treatment Indication and the Cardiac Surgery Indication. Each of the Dose Escalation studies for the two indications shall be conducted in accordance with the following parameters:

(a) Each shall be a four (4) arm study with up to fifty (50) study subjects in each arm;

(b) The four (4) arms of each study shall be (i) Dose Escalation of rFXIII alone, (ii) Dose Escalation of rFVIIa alone, (iii) Dose Escalation of Combination rFVIIa/rFXIII, and (iv) placebo; *provided, however*, that if requested by the applicable Regulatory Agency or otherwise made necessary by clinical feasibility, Dose Escalation of Combination rFVIIa/rFXIII may be performed after Dose Escalation of rFXIII alone and Dose Escalation of rFVIIa alone, *provided further* that an arm for the Dose Escalation study for rFVIIa in the Cancer Treatment Indication need not be performed because of the prior studies conducted by NN, the results of which have been disclosed to ZGEN and *provided further*, that the Parties acknowledge that an arm for the Dose Escalation study for rFVIIa in the Cardiac Surgery Indication has been commenced by NN; and

(c) The Primary Endpoint for each study shall be safety, as measured by the incidence and severity of adverse events compared to placebo.

If the Dose Escalation study of Combination rFVIIa/rFXIII is delayed, NN may consider and decide whether to proceed with a three (3) arm CPOC Study (i.e., without the Combination rFVIIa/rFXIII arm). If NN decides to proceed with a three (3) arm CPOC Study, the Parties will, in good faith, discuss and make appropriate adjustments under this **Article 3**.

Upon conclusion of the Dose Escalation study and in accordance with **Sections 6.2** and **6.3**, NN shall provide and discuss with ZGEN information related to the Dose Escalation study.

Section 3.4. **Clinical Proof of Concept Study Requirement.** Subject to **Section 3.2(e)**, NN shall conduct a CPOC Study for each of the Cancer Treatment Indication and the Cardiac Surgery Indication. Each of the CPOC Studies shall be conducted in accordance with the following parameters:

(a) Each shall be a parallel, four (4) arm study utilizing an optimal dose for each arm and shall be adequately powered versus placebo to at least eighty percent (80%), but in any event not to exceed one hundred (100) study subjects in each arm unless NN, in its sole discretion, decides otherwise;

(b) The four (4) arms of each CPOC Study shall be (i) rFXIII alone, (ii) rFVIIa alone, (iii) Combination rFVIIa/rFXIII, and (iv) placebo;

(c) The Primary Endpoint for each CPOC Study shall be efficacy in stopping or reducing bleeding;

(d) For the Cardiac Surgery Indication CPOC Study, efficacy in stopping or reducing bleeding shall be determined, at NN's decision, as (i) the amount of blood lost by the study subject, such as by drain volume, (ii) the number and/or volume/quantity of packed red blood cell transfusions required by the study subject, or (iii) some reasonable combination of **Section 3.4(d)(i)** and **3.4(d)(ii)**;

(e) For the Cancer Treatment Indication CPOC Study, efficacy in stopping or reducing bleeding shall be determined, at NN's decision, as (i) a qualitative clinical bleeding evaluation for each study

subject, (ii) the number and quantity of packed red blood cell transfusions required by the study subject, or (iii) some reasonable combination of **Section 3.4(e)(i)** and **3.4(e)(ii)**;

(f) For each of the CPOC Studies, state-of-the-art techniques and technology shall be used in estimating blood loss and determining or evaluating whether bleeding has been stopped or reduced; and

(g) At the conclusion of each CPOC Study, the data from the study shall be analyzed to determine if CPOC has been achieved for each active arm of the study and NN shall inform ZGEN of the results pursuant to **Sections 6.2** and **6.3**. CPOC shall be deemed to have been achieved if (i) the results from the active arm compared to the placebo arm, based on the Primary Endpoint for the study, show a statistical significance of P<0.05 (1-sided testing) and (ii) no significant safety concerns have been identified by the Data Monitoring Committee for the active arm.

Section 3.5. **Superiority Assessment; Statistical Analysis of CPOC Study Results.** If two (2) or more arms achieved CPOC in a CPOC Study described in **Section 3.4**, NN shall conduct a statistical analysis of the results of the CPOC Study with respect to such products in accordance with the following parameters:

(a) If CPOC was achieved for each of rFXIII and rFVIIa, a superiority assessment of rFXIII compared to rFVIIa shall be performed comparing the efficacy results from the rFXIII arm with the rFVIIa arm. If the results of the CPOC Study based on the Primary Endpoint show that the rFXIII arm is superior to the rFVIIa arm with P<0.10 (2-sided testing), then rFXIII shall be deemed to be superior to rFVIIa;

(b) If CPOC was achieved for each of rFXIII and rFVIIa, a superiority assessment of rFVIIa compared to rFXIII shall be performed comparing the efficacy results from the rFVIIa arm with the rFXIII arm. If the results of the CPOC Study based on the Primary Endpoint show that the rFVIIa arm is superior to the rFXIII arm with P<0.10 (2-sided testing), then rFVIIa shall be deemed to be superior to rFXIII;

(c) If CPOC was achieved for each of rFVIIa and Combination rFVIIa/rFXIII, a superiority assessment of Combination rFVIIa/rFXIII compared to rFVIIa shall be performed comparing the efficacy results from the Combination rFVIIa/rFXIII arm with the rFVIIa arm. If the results of the CPOC Study based on the Primary Endpoint show that the Combination rFVIIa/rFXIII arm is superior to the rFVIIa arm with P<0.10 (2-sided testing), then Combination rFVIIa/rFXIII shall be deemed to be superior to rFVIIa; and

(d) If CPOC was achieved for each of rFXIII and Combination rFVIIa/rFXIII, a superiority assessment of Combination rFVIIa/rFXIII compared to rFXIII shall be performed comparing the efficacy results from the Combination rFVIIa/rFXIII arm with the rFXIII arm. If the results of the CPOC Study based on the Primary Endpoint show that the Combination rFVIIa/rFXIII arm is superior to the rFXIII arm with P<0.10 (2-sided testing), then Combination rFVIIa/rFXIII shall be deemed to be superior to rFXIII.

Upon conclusion of the Statistical Analysis and in accordance with **Sections 6.2** and **6.3**, NN shall provide and reasonably discuss with ZGEN the results of the Statistical Analysis.

Section 3.6. **Phase III Development Candidate.** If only one of rFXIII or Combination rFVIIa/rFXIII achieved CPOC in the CPOC Study described in **Section 3.4** for an indication, it shall be the Phase III Development Candidate for the indication (i.e., Cardiac Surgery Indication or Cancer Treatment Indication). If more than one product achieved CPOC in a CPOC Study described in **Section 3.4** for an indication, the product that shall be the Phase III Development Candidate for the indication shall be established according to the following criteria based on the Statistical Analysis performed in **Section 3.5** for establishing a "superior" product and applying the rule that a product that has achieved CPOC shall automatically be deemed to be "superior" to a product that has not achieved CPOC:

(a) If (i) rFXIII is superior to rFVIIa and (ii) Combination rFVIIa/rFXIII is not superior to rFXIII, then rFXIII shall be the Phase III Development Candidate;

(b) If (i) Combination rFVIIa/rFXIII is superior to rFVIIa and (ii) Combination rFVIIa/rFXIII is superior to rFXIII, then Combination rFVIIa/rFXIII shall be the Phase III Development Candidate;

(c) If (i) rFXIII achieves CPOC, (ii) rFVIIa is superior to rFXIII, and (iii) Combination rFVIIa/rFXIII is not superior to rFVIIa, then no Phase III Development Candidate needs to be established for the applicable indication and NN shall have no further development obligations with respect to Licensed Products for such indication, *provided, however*, that in such case, NN may, in its sole discretion, select rFVIIa as the Phase III Development Candidate;

(d) If (i) rFXIII did not achieve CPOC and either (ii) Combination rFVIIa/rFXIII does not achieve CPOC or (iii) Combination rFVIIa/rFXIII is not superior to rFVIIa, then no Phase III Development Candidate needs to be established for the applicable indication and NN shall have no further development obligations with respect to Licensed Products for such indication, *provided, however*, that in such case, NN may, in its sole discretion, select rFVIIa as the Phase III Development Candidate; and

(e) In all other cases in which no product is superior, NN shall select, within a reasonable time after completion of the Statistical Analysis in **Section 3.5**, either rFXIII or rFVIIa as the Phase III Development Candidate based on NN's commercial considerations.

It is recognized that it is possible that different products may be established as the Phase III Development Candidate for each of the two indications. NN shall promptly inform ZGEN of the Phase III Development Candidate for each indication.

The method for establishing the Phase III Development Candidate described in this **Section 3.6** is designed to capture, refine, clarify and supplement the outline set forth in **Exhibit H** attached to this Agreement that the Parties had used to negotiate this Agreement. In the event of any conflict or inconsistency between **Exhibit H** and the provisions of this **Section 3.6**, this **Section 3.6** shall prevail.

Section 3.7. **Conduct of Phase III Clinical Trials.** NN shall conduct Phase III Clinical Trials for the Cardiac Surgery Indication and Cancer Treatment Indication using the Phase III Development Candidates established pursuant to **Section 3.6**. Each Phase III Clinical Trial shall be conducted using a two (2) arm parallel design and shall include an adequate number of study subjects based on the Primary Endpoint. Subject to consultation with the applicable Regulatory Agency, the Primary Endpoints for the Phase III Clinical Trials for the Cardiac Surgery Indication and the Cancer Treatment Indication shall be similar to the Primary Endpoints used in the CPOC Studies pursuant to **Section 3.4** for the Cardiac Surgery Indication and the Cancer Treatment Indication, respectively. It is recognized that, in the event that the applicable Regulatory Agency requires a Primary Endpoint for either Phase III Clinical Trial that is not similar to the Primary Endpoint used for the corresponding CPOC Study and such requirement delays the start of the Phase III Clinical Trial, then the Time Milestones (as defined in **Section 4.2**) shall be delayed pursuant to **Section 4.2(e)(iv)**.

Section 3.8. **Regulatory Filings.** NN shall be solely responsible for the filing of and shall be the sole owner of all clinical trial applications and Marketing Applications for Licensed Products filed with any Regulatory Agency in any jurisdiction after the Effective Date.

Section 3.9. **Manufacturing and Clinical Supplies.** Subject to the provisions of **Section 5.5** with respect to Licensed Products to be supplied by ZGEN to NN, NN shall be solely responsible for the manufacture of Licensed Products as needed to meet its development and commercialization obligations under this Agreement.

NN, at its sole discretion, may manufacture Licensed Products itself or utilize one or more contract manufacturing organizations for such manufacture.

Section 3.10. **Commercialization.** NN shall be solely responsible, at its sole discretion and cost, for all sales and marketing activities for Licensed Products. NN shall employ resources and efforts in promoting, marketing and selling Licensed Products that are consistent with its activities (and the activities of its Affiliates, including Novo) with respect to its other products of similar profit potential and product profile. NN, at its sole discretion and cost, shall develop trademarks and trade dress for Licensed Products and shall be the owner of all such trademarks and trade dress.

Section 3.11. **Improvements.** Nothing in this Agreement shall prevent or prohibit NN from discovering or conceiving of, or filing patent applications with respect to, any improvements made by NN related to rFXIII, including new methods of use, formulations, combinations or other inventions.

Article 4
Fees and Royalties

Section 4.1. **Signature Fee.** NN shall pay to ZGEN a signature fee of thirteen million United States dollars (U.S. $13,000,000) (the "**Signature Fee**") within five (5) business days of the execution of this Agreement by the Parties and Novo. No part of the Signature Fee shall be refundable, nor may any part be credited against any other amounts payable under this Agreement or otherwise.

Section 4.2. **Milestone Fees.** NN shall pay to ZGEN the milestone fees set forth in **Sections 4.2(a)** through **4.2(d)**, subject to utilization of any credits provided in **Sections 4.5(b)** and **5.5**. Each milestone fee shall be paid within thirty (30) days after the indicated milestone event has been achieved by NN or its Affiliate or Sublicensee (**"Event Milestone"**) or on or before the milestone date (if a milestone date is shown) (**"Time Milestone"**), whichever occurs first; *provided, however,* that a Time Milestone associated with an Event Milestone and milestone fee may be delayed or terminated pursuant to **Section 4.2(e)**. Each milestone fee shall be payable only once; no additional milestone fee for a given indication shall be payable for repeated achievement of the Event Milestone or subsequent achievement of the Time Milestone associated with the Event Milestone and milestone fee. No part of the milestone fee shall be refundable. Except as set forth in **Sections 4.2(b)(*), 4.2(c)(*), 4.5(b), 5.5(c)** and **5.5(d)**, no part of the milestone fee shall be credited against any other amount payable under this Agreement or otherwise.

(a) The milestone fees for the Congenital Factor XIII Deficiency shall be as follows:

	Earlier of:	
Milestone Fee	**Event Milestone**	**Time Milestone (Subject to Section 4.2(e))**
U.S. $3,100,000	FPFV in first Phase III Clinical Trial of a Licensed Product	March 25, 2006
U.S. $4,650,000	First filing for Marketing Approval in the United States or European Union for a Licensed Product	September 25, 2008
U.S. $7,750,000	First Marketing Approval in the United States or European Union for a Licensed Product	None

(b) The milestone fees for the Cardiac Surgery Indication shall be as follows:

		Earlier of:	
Milestone Fee	**Milestone Fee if Licensed Product for Congenital Factor XIII Deficiency Not Developed Due to Section 3.2(b)(*)**	**Event Milestone**	**Time Milestone (subject to Section 4.2(e))**
U.S. $3,255,000	U.S. $4,371,000	FPFV in first Dose Escalation study for a Factor XIII Product or Combination Product	June 25, 2006
U.S. $2,170,000	U.S. $2,914,000	FPFV in CPOC Study	September 25, 2007
U.S. $6,510,000	U.S. $8,742,000	Achievement of CPOC by a Factor XIII Product or Combination Product (**)	March 25, 2009
U.S. $3,255,000	U.S. $4,371,000	Decision to Submit Registration File for a Factor XIII Product or Combination Product	September 25, 2010
U.S. $6,510,000	U.S. $8,742,000	First Marketing Approval for a Factor XIII Product or Combination Product	None

(*) If the lower milestone fee has been paid as a result of an Event Milestone or Time Milestone occurring prior to termination of the development of a Licensed Product for Congenital Factor XIII Deficiency pursuant to **Section 3.2(b)** (e.g., FPFV in the Dose Escalation study or the related Time Milestone has occurred prior to such termination), then NN shall promptly pay ZGEN an amount, which when added to the earlier milestone fee, would equal the higher milestone fee due as a result of such termination under **Section 3.2(b)**; *provided, however,* that any such amount shall be reduced by the amount previously paid to ZGEN by NN for any Event Milestone or Time Milestone for the Congenital Factor XIII Deficiency pursuant to **Section 4.2(a).**

(**) Upon achievement of this Event Milestone in a CPOC Study pursuant to **Section 3.4** prior to the associated Time Milestone the associated milestone fee to be paid for such Event Milestone shall be adjusted in two special situations to be: (i) fifty percent (50%) of the associated milestone fee in the table if **Section 3.6(c)** applies to the indication and (ii) zero ($0.00) if **Section 3.6(d)** applies to the indication, to the extent such special determinations under **Sections 3.6(c)** and **3.6(d)** can be made prior to the Time Milestone. Notwithstanding the first paragraph of this Section 4.2, such milestone fee shall not be payable by NN until the earlier of: (A) the Time Milestone (payment of unadjusted milestone fee) or (B) the later of (I) thirty (30) days from the achievement of such Event Milestone or (II) ten (10) days following the completion of the superiority assessments under **Section 3.5** that are necessary to determine whether **Section 3.6(c)** or **3.6(d)** apply to the indication (payment of adjusted or unadjusted milestone fee). However, if NN thereafter initiates a Phase III Clinical Trial or achieves CPOC in another CPOC Study for a Factor XIII Product or Combination Product for such indication, the balance of the full milestone fee set forth in the table for such Event Milestone that has not been paid shall become payable.

(c) The milestone fees for the Cancer Treatment Indication shall be as follows:

		Earlier of:	
Milestone Fee	**Milestone Fee if Licensed Product for Congenital Factor XIII Deficiency Not Developed Due to Section 3.2(b)(*)**	**Event Milestone**	**Time Milestone (subject to Section 4.2(e))**
U.S. $3,720,000	U.S. $4,929,000	FPFV in first Dose Escalation study for a Factor XIII Product or Combination Product	June 25, 2006
U.S. $2,480,000	U.S. $3,286,000	FPFV in CPOC Study	September 25, 2007
U.S. $7,440,000	U.S. $9,858,000	Achievement of CPOC by a Factor XIII Product or Combination Product (**)	March 25, 2009
U.S. $3,720,000	U.S. $4,929,000	Decision to Submit Registration File for a Factor XIII Product or Combination Product	September 25, 2010
U.S. $7,440,000	U.S. $9,858,000	First Marketing Approval for a Factor XIII Product or Combination Product	None

(*) If the lower milestone fee has been paid as a result of an Event Milestone or Time Milestone occurring prior to termination of the development of a Licensed Product for Congenital Factor XIII Deficiency pursuant to **Section 3.2(b)** (e.g., FPFV in the Dose Escalation study or the related Time Milestone has occurred prior to such termination), then NN shall promptly pay ZGEN an amount, which when added to the earlier milestone fee, would equal the higher milestone fee due as a result of such termination under **Section 3.2(b)**; *provided, however,* that any such amount shall be reduced by the amount previously paid to ZGEN by NN for any Event Milestone or Time Milestone for the Congenital Factor XIII Deficiency pursuant to **Section 4.2(a).**

(**) Upon achievement of this Event Milestone in a CPOC Study pursuant to **Section 3.4** prior to the associated Time Milestone the associated milestone fee to be paid for such Event Milestone shall be adjusted in two special situations to be: (i) fifty percent (50%) of the associated milestone fee in the table if **Section 3.6(c)** applies to the indication and (ii) zero ($0.00) if **Section 3.6(d)** applies to the indication, to the extent such special determinations under **Sections 3.6(c)** and **3.6(d)** can be made prior to the Time Milestone. Notwithstanding the first paragraph of this Section 4.2, such milestone fee shall not be payable by NN until the earlier of: (A) the Time Milestone (payment of unadjusted milestone fee) or (B) the later of (I) thirty (30) days from the achievement of such Event Milestone or (II) ten (10) days following the completion of the superiority assessments under **Section 3.5** that are necessary to determine whether **Section 3.6(c)** or **3.6(d)** apply to the indication (payment of adjusted or unadjusted milestone fee). However, if NN thereafter initiates a Phase III Clinical Trial or achieves CPOC in another CPOC Study for a Factor XIII Product or Combination Product for such indication, the balance of the full milestone fee set forth in the table for such Event Milestone that has not been paid shall become payable.

(d) In the event that NN selects rFVIIa as the Phase III Development Candidate for the Cardiac Surgery Indication or Cancer Treatment Indication pursuant to **Section 3.6(e)**, then NN shall pay milestone fees with respect to an rFVIIa product based on Event Milestones and Time Milestones for the indication that are the same as the Event Milestones and Time Milestones in the applicable table in **Section 4.2(b)** or **4.2(c)** as if the rFVIIa product were a Factor XIII Product; however, the related milestone fees shall be: (i) for the achievement of Decision to Submit Registration File for an rFVIIa product—two times (2x) the corresponding

amount in the table; and (ii) for receipt of first Marketing Approval for an rFVIIa product—two and one-half times (2½ x) the corresponding amount in the table.

(e) With respect to the Time Milestones associated with the Event Milestones and milestone fees in the tables in **Sections 4.2(a), 4.2(b), 4.2(c)** and **4.2(d)**:

(i) The Time Milestones in the applicable table in **Section 4.2(a), 4.2(b)** or **4.2(c)** for an indication shall terminate if the Licensed Product or rFVIIa product in the case of **Section 4.2(d)** for the indication is terminated pursuant to **Section 3.2(e)**, and the Time Milestones in the table in **Section 4.2(a)** shall terminate if a Factor XIII Product for Congenital Factor XIII Deficiency is terminated pursuant to **Section 3.2(b)**;

(ii) The Time Milestone associated with the Decision to Submit Registration File shall not apply if no Phase III Development Candidate needs to be established with respect to the indication pursuant to **Section 3.6(c)** or **Section 3.6(d)**;

(iii) In the event ZGEN does not transfer the information and materials pursuant to **Section 5.1** by the Technology Transfer Dates, the Time Milestones in the tables in **Sections 4.2(a), 4.2(b)** and **4.2(c)** shall be delayed by the actual amount of time lost in development of the Licensed Product or rFVIIa product in the case of **Section 4.2(d)** for the particular indication as a result of the transfer occurring after the Technology Transfer Dates despite NN's exercise of commercially reasonable efforts. NN shall notify ZGEN as soon as it appears that there could be a delay in development as a result of a delay in such transfer and shall provide and discuss with ZGEN information regarding the situation and NN's efforts to overcome or reduce any delay. In the event of a dispute between the Parties regarding the actual amount of delay to be added to the Time Milestones, either Party may request that the matter be referred to the Chief Executive Officers of ZGEN and NN to be resolved, if at all, in the next forty-five (45) days and NN shall promptly provide each of the Chief Executive Officers with information regarding the situation, its estimate of the actual amount of time lost in development and NN's efforts to overcome or reduce any delay; and

(iv) In the event that development of a Licensed Product, or the development of an rFVIIa product pursuant to **Section 3.6(e)**, for the Congenital Factor XIII Deficiency, Cardiac Surgery Indication or Cancer Treatment Indication is delayed due to a Regulatory Event or a technical issue, including feasibility, safety, CMC and toxicology issues, which delay cannot be overcome or reduced by NN's commercially reasonable efforts, then the date for the Time Milestone associated with the affected Event Milestone shall be postponed for the period of time of the delay. NN shall notify ZGEN as soon as is reasonably practicable following the occurrence of the Regulatory Event or technical issue that could reasonably be expected to cause such a delay and shall provide ZGEN with information (to the extent available at the time) regarding the situation, including NN's preliminary assessment, efforts and estimated time to complete a full assessment. Thereafter, NN shall provide ZGEN, from time to time, with any further information regarding the situation and NN's on-going assessment and efforts. For the avoidance of doubt, this clause (iv) can be applied to (but is not limited to) the Time Milestone associated with the Decision to Submit Registration File in the event there is a delay in the start of a Phase III Clinical Trial that is caused by the FDA or EMEA requiring a Primary Endpoint for a Phase III Clinical Trial that is not similar to the Primary Endpoint used for the corresponding CPOC Study.

(f) For the avoidance of doubt, it is acknowledged by the Parties with respect to rFVIIa that (i) no milestone fee shall be payable to ZGEN with respect to the development of rFVIIa for Congenital Factor XIII Deficiency or any other indication, except as provided in **Section 4.2(d)** with respect to the Cardiac Surgery Indication or Cancer Treatment Indication, and (ii) any Time Milestones related to the development of rFVIIa for the Cardiac Surgery Indication or Cancer Treatment Indication pursuant to **Section 4.2(d)** may be terminated or adjusted as provided in **Section 4.2(e)**.

(g) For the avoidance of doubt, it is acknowledged by the Parties that, in the event NN has no further development obligations with respect to an indication pursuant to **Section 3.6(c)** or **Section 3.6(d)**, NN shall not be obligated to select a Phase III Development Candidate and, as provided in **Section 4.2(e)(ii)**, the Time Milestones related to that indication shall terminate.

(h) The basis for paying milestone fees described in this **Section 4.2** is designed to capture, refine, clarify and supplement the outline set forth in **Exhibit H** attached to this Agreement that the Parties had used to negotiate this Agreement. In the event of any conflict or inconsistency between **Exhibit H** and the provisions of this **Section 4.2**, this **Section 4.2** shall prevail.

It is recognized and agreed that despite the termination of a development obligation for an indication pursuant to **Sections 3.2(b)**, **3.2(e)**, **3.6(c)** or **3.6(d)**, a milestone fee will be payable if a Licensed Product eventually achieves an Event Milestone for the indication. For the avoidance of doubt, only the Congenital Factor XIII Deficiency indication, Cardiac Surgery Indication and Cancer Treatment Indication can cause milestone fees to become payable.

Section 4.3. **Royalties.** NN shall pay to ZGEN a royalty on Net Sales of each Licensed Product, as follows:

(a) For each Factor XIII Product that is a Patent Product, NN shall pay ZGEN royalties equal to eleven percent (11%) of Net Sales of such Factor XIII Product. The royalties shall be increased to twelve percent (12%) of Net Sales of all such Factor XIII Products in the event that:

(i) a Factor XIII Product gains Marketing Approval in the United States or European Union for the treatment of Congenital Factor XIII Deficiency or a Licensed Product gains Marketing Approval for an additional indication other than for the treatment of Congenital Factor XIII Deficiency, the Cancer Treatment Indication or the Cardiac Surgery Indication;

(ii) a Licensed Product gains Marketing Approval for treatment of the Cardiac Surgery Indication or NN selects rFVIIa as the Phase III Development Candidate for such indication pursuant to **Section 3.6(e)**;

(iii) a Licensed Product gains Marketing Approval for treatment of the Cancer Treatment Indication or NN selects rFVIIa as the Phase III Development Candidate for such indication pursuant to **Section 3.6(e)**; and

(iv) a Licensed Product gains Marketing Approval for an indication other than for the treatment of Congenital Factor XIII Deficiency, the Cancer Treatment Indication, the Cardiac Surgery Indication or the additional indication, if applicable, set forth in clause (i) of this **Section 4.3(a)**.

(b) For each Combination Product that is a Patent Product, NN shall pay ZGEN royalties equal to five and one-half percent (5.5%) of Net Sales of such Combination Product. The royalties shall be increased to six percent (6.0%) of Net Sales of all such Combination Products in the event that:

(i) a Factor XIII Product gains Marketing Approval in the United States or European Union for the treatment of Congenital Factor XIII Deficiency or a Licensed Product gains Marketing Approval for an additional indication other than for the treatment of Congenital Factor XIII Deficiency, the Cancer Treatment Indication or the Cardiac Surgery Indication;

(ii) a Licensed Product gains Marketing Approval for treatment of the Cardiac Surgery Indication or NN selects rFVIIa as the Phase III Development Candidate for such indication pursuant to **Section 3.6(e)**;

(iii) a Licensed Product gains Marketing Approval for treatment of the Cancer Treatment Indication or NN selects rFVIIa as the Phase III Development Candidate for such indication pursuant to **Section 3.6(e)**; and

(iv) a Licensed Product gains Marketing Approval for an indication other than for the treatment of Congenital Factor XIII Deficiency, the Cancer Treatment Indication, the Cardiac Surgery Indication or the additional indication, if applicable, set forth in clause (i) of this **Section 4.3(b)**.

(c) NN's obligation to pay royalties for a Patent Product shall cease on a country-by-country basis on the expiration date of the last-to-expire of any patent included in the Licensed Patents or Sublicensed Patents (or in the case of only a patent application included therein, seven and one-half (7.5) years after the initial filing of such application) with a Patent Claim which would be infringed, in the absence of the licenses granted under this Agreement, by the making, using, importation, offer for sale or sale of the Patent Product (i.e., when the Patent Product ceases being a "**Patent Product**" as defined in **Section 1.40** and thereafter may become a "**Know-How Product**").

(d) For each Factor XIII Product or Combination Product that is a Know-How Product, NN shall pay ZGEN royalties equal to five percent (5.0%) of Net Sales of such Factor XIII Product and two and one-half percent (2.5%) of Net Sales of such Combination Product. NN's obligation to pay royalties for each Know-How Product shall expire with respect to Net Sales in each country occurring after the earlier of: (i) fifteen (15) years after the First Commercial Sale of the Licensed Product in such country or (ii) December 31, 2023.

(e) For the avoidance of doubt, no royalties shall be paid with respect to the sales of rFVIIa.

Section 4.4. **Payments Under UW Agreement/Aventis Agreement.** ZGEN shall pay to UW, when due, all amounts due under the UW Agreement. NN shall pay to Aventis, when due, all royalties due under the Aventis Agreement and the milestone fee due pursuant to **Section 4.3** of the Aventis Agreement.

Section 4.5. **Other Licenses and Royalty Offset.**

(a) NN shall be solely responsible for determining whether or not additional licenses must be taken in order to commercialize Licensed Products in accordance with this Agreement and for the payment of any royalties and other fees required by such licenses. Except as set forth in **Section 4.5(b)**, NN shall pay to ZGEN the royalties set forth in **Section 4.3** regardless of whether a license to any other patents or other rights is required to commercialize a Licensed Product or whether royalties or other fees must be paid to other parties. For the avoidance of doubt and except as set forth in **Section 4.5(b)**, NN shall not be entitled to offset the royalties or fees paid by it to other parties, whether in connection with licenses or otherwise, against the royalties, milestones or other payments due and owing to ZGEN under this Agreement.

(b) NN may offset any royalties paid to Aventis under the Aventis Agreement against royalties payable to ZGEN hereunder. NN may offset the milestone paid to Aventis pursuant to **Section 4.3** of the Aventis Agreement against any milestone fee coming due ZGEN following such payment to Aventis.

Section 4.6. **Taxation of Payments.** ZGEN shall be responsible for and shall bear any taxes levied upon payments received by ZGEN, and ZGEN hereby authorizes NN to withhold such taxes from the payments which are payable to ZGEN in accordance with this Agreement if NN is either required to do so under the applicable tax laws or directed to do so by an agency of the relevant government. Upon ZGEN's written request, NN shall, with respect to the laws of Denmark/Switzerland, reasonably support ZGEN in its legal efforts to minimize any such withholding taxes, and provide ZGEN with information about and necessary for any documentation needed to reduce withholding to a legal minimum.

Section 4.7. **Currency Blockage.** If the laws or regulations of another country prevent the conversion of its currency into United States dollars for the payment of royalties, NN will either (a) pay such royalties by depositing the currency of the other country into a bank account designated by ZGEN in that country or (b) if permitted by law, pay such royalties in the currency of the country in question to ZGEN's designee in that country.

Section 4.8. **Wire Transfer.** All payments to be made by NN to ZGEN under this Agreement shall be made by wire transfer from NN to the following account of ZGEN:

Bank of America
Commercial Banking Account
Seattle, WA 98104
ABA routing number: 026009593
Account number: 62140512

Section 4.9. **Acknowledgment.** NN acknowledges that the Licensed Know-How, regulatory filings, supply contracts, clinical supplies, biological materials, reagents, assays, protocols, SOPs and information/documents to be provided under this Agreement constitute valuable intellectual property, trade secrets, know-how, filings, rights, information/documents and materials of ZGEN. The Parties acknowledge and agree that, for their mutual convenience and after considering other alternatives, the payments to ZGEN set forth in this Agreement, including this **Article 4**, and the timing of and basis for the payments (including the milestone fees and the period during which royalties are due) are an appropriate and mutually convenient way of compensating ZGEN.

Section 4.10. **Annual License Fee.** In the event that during any nine (9) month period:

(a) ZGEN is not entitled to receive any milestone fees under **Section 4.2** because, during such nine (9) month period, an Event Milestone was not achieved and a Time Milestone did not occur;

(b) ZGEN is not receiving royalty payments under **Article 4** related to a Licensed Product for the treatment of any indication;

(c) NN is not conducting a development program pursuant to **Article 3** for a Licensed Product for the treatment of Congenital Factor XIII Deficiency, the Cancer Treatment Indication or the Cardiac Surgery Indication for which a milestone fee could become payable because all such programs have been completed, terminated pursuant to **Sections 3.2(b)**, **3.2(e)**, **3.6(c)** or **3.6(d)**; for the avoidance of doubt, if such a program is delayed pursuant to **Section 4.2(e)(iii)** or **(iv)**, so long as NN is using commercially reasonable efforts to overcome or reduce the delay, the Parties acknowledge that NN is conducting such program and this **Section 4.10(c)** is not satisfied; and

(d) NN is not conducting an active and vigorous drug research and development program, including meeting and fulfilling milestones and goals in accordance with NN's internal guidelines for research and development programs, for a Licensed Product for the treatment of an indication other than Congenital Factor XIII Deficiency, the Cancer Treatment Indication or the Cardiac Surgery Indication;

then NN, at its option, shall irrevocably elect no later than thirty (30) days after the expiration of the nine (9) month period to either (i) pay ZGEN an annual license fee of one million United States dollars (U.S. $1,000,000) immediately upon expiration of the nine (9) month period and on each annual anniversary thereof until the expiration date of the last-to-expire patent within the Licensed Patents and Sublicensed Patents or (ii) terminate this Agreement by giving ZGEN sixty (60) days' prior written notice of termination. In the event NN does not make a timely election, it shall be deemed to have elected to pay the annual license fee pursuant to clause (i) of the preceding sentence. For the avoidance of doubt, if NN begins paying the milestone payments or royalty payments set forth in paragraphs (a) or (b) above or establishes a development program as set forth in paragraphs

(c) or (d) above as reasonably demonstrated to ZGEN, for at least six (6) months prior to the next due date of the next annual license fee, then the next annual license fee shall not be payable to ZGEN and subsequent annual license fees shall not be payable if, during the six (6) months prior to the due date of an annual license fee, such milestones and royalties are being paid or such development programs are being conducted.

Section 4.11. Payments and Reports. Royalties payable pursuant to this Agreement shall be due quarterly within forty-five (45) days following the end of each Calendar Quarter for Net Sales in such Calendar Quarter. All sales in non-United States currencies shall be converted into United States dollars using the rate of exchange quoted by Bank of America and its successor(s) on the last business day of the Calendar Quarter in which the sales were made. Each such payment shall be accompanied by a statement of Net Sales for the quarter (including number of units), applicable exchange rates and the calculation of royalties payable hereunder by Licensed Product and country. Such statement shall also include the royalties and milestone paid or payable to Aventis under the Aventis Agreement, the information to be provided Aventis in connection with such payment and the method for applying the offset pursuant to **Section 4.5(b)** to amounts otherwise due ZGEN hereunder. All milestone fees, royalties and all other amounts which are overdue under this Agreement will bear interest at the rate of one and one-half percent (1½%) per month from the date due through the date of payment. NN shall keep, and shall cause its Affiliates and Sublicensees to keep, complete, true and accurate records for at least five (5) years for the purpose of showing the derivation of all milestone fees and royalties payable under this Agreement. Independent accountants engaged on behalf of ZGEN, who are reasonably acceptable to NN, shall have the right to inspect and audit such records at any time during reasonable business hours upon reasonable prior notice to NN or any of its Affiliates or Sublicensees, but such right will not be exercised more often than annually (it being understood that a single exercise of such right may include a series of related or continuing inspections and audits). The cost of such inspection and audit shall be borne by ZGEN unless there is a discrepancy of greater than, or equal to, ten percent (10%) in NN's favor in which case NN shall bear the entire cost of the inspection and audit.

Article 5
Technology Transfer, ZGEN Services and rFXIII Supply

Section 5.1. Transfer. The Technology Transfer Letter sets forth the documents, files and materials that constitute Licensed Know-How that ZGEN expects to transfer to NN, which transfer shall be completed by the Technology Transfer Date for each item; *provided, however*, that ZGEN shall not be responsible for delays in transfer that are out of its control. It is recognized and agreed that (i) most documents and files to be transferred hereunder will be transferred via electronic media, (ii) those materials in the possession or control of ZGEN at the Effective Date will be delivered to NN at their current locations, (iii) if, following the execution of this Agreement, NN indicates a preference for certain of those materials not in ZGEN's possession at the Effective Date to remain at any outside contractor, ZGEN's obligation to transfer those certain materials to NN shall be deemed fulfilled upon notification of the contractor (with copies to NN) that responsibility for such materials has been transferred to NN.

Section 5.2. Validation of Assays. ZGEN has established assays for testing and release of rFXIII bulk drug substance and for testing and release of rFXIII drug product. ZGEN shall validate the assays for manufacturing release of rFXIII bulk drug substance and rFXIII drug product for Phase III Clinical Trials and commercial sales according to protocols (including acceptance criteria) that have been forwarded to NN by ZGEN, subject to such modifications as were agreed upon and confirmed in writing by the Parties on or immediately prior to the Effective Date, and using non-GMP material. For such work (including testing of GMP manufacturing runs and preparation of certificates of analysis) by ZGEN after the Effective Date, NN shall pay ZGEN, on a quarterly basis, at the rate of $290,000 per FTE for ZGEN's personnel who are involved with the project and reimburse ZGEN, on a monthly basis, for any subcontractors' costs and reasonable travel costs.

Section 5.3 Stability Testing Program. ZGEN and its subcontractors shall continue already-initiated stability testing programs until the date designated by NN to ZGEN as being the date upon which NN

wishes to take over such programs. For such work, NN shall pay ZGEN, on a quarterly basis, at the rate of $290,000 per FTE for ZGEN's personnel who are involved with the project and reimburse ZGEN, on a monthly basis, for any subcontractors' costs and reasonable travel costs.

Section 5.4 **ZGEN Services**. ZGEN shall undertake the following services for NN:

(a) At NN's cost, provide up to two (2) representatives acceptable to NN to participate with NN in the first investigator's meeting with respect to the Cardiac Surgery Indication following the Effective Date and to provide reasonable assistance to NN in preparation work conducted by NN for such meeting.

(b) At NN's cost, provide up to (2) two representatives from each of preclinical and clinical development to consult and provide advice to NN regarding NN's preparation for any meeting with a Regulatory Agency regarding Congenital Factor XIII Deficiency during 2004 and 2005 (including, at NN's request, to attend such meeting); *provided, however,* that ZGEN's personnel shall not be obliged to spend more than sixty (60) hours in the aggregate during 2005 in the provision of such support.

(c) At ZGEN's cost, update the rFXIII Investigational Brochure within five (5) days after the Effective Date in ZGEN's format with information reasonably sufficient to fulfill the requirements of ICH E6 "Guideline for Good Clinical Practice", Section 7.0, Investigators' Brochure, Step 4, June 1996. NN shall then submit an updated version in NN's preferred format to the FDA within the time period required by applicable regulations.

(d) At ZGEN's cost, finalize the Congenital Factor XIII Deficiency annual report to the FDA by October 17, 2004 in ZGEN's format with information reasonably sufficient to fulfill the requirements of 21CFR Part 312.33. NN shall then submit the updated report in NN's preferred format to the FDA within the time period required by applicable regulations.

(e) At ZGEN's cost, finalize and submit for publication by December 31, 2004 certain manuscripts as specified in the Manuscripts Letter.

For purposes of **Section 5.4(a)** and **Section 5.4(b)** only, in 2004, NN's costs shall mean reimbursement of ZGEN, on a monthly basis, for any reasonable out-of-pocket expenses incurred by ZGEN in 2004, including any travel expenses, and in 2005, NN's costs shall mean reimbursement of ZGEN, on a monthly basis, for any reasonable travel expenses, and payment to ZGEN, on a quarterly basis, for any activities performed by ZGEN personnel in 2005 at the rate of $290,000 per FTE.

Section 5.5. **Supply of rFXIII**

(a) NN hereby purchases from ZGEN, and ZGEN hereby sells to NN, the amount and form of Recombinant Factor XIII produced by Avecia that is described in **Exhibit I** (**"rFXIII Supplies"**). Title to the rFXIII Supplies shall transfer to NN upon the Effective Date, and NN shall be responsible for any storage costs incurred after the Effective Date. Release of the rFXIII Supplies shall be the responsibility of, and under the control of, NN. The rFXIII Supplies are delivered to NN at their current locations.

(b) Within five (5) business days of the Effective Date, NN shall pay to ZGEN two million United States dollars (U.S. $2,000,000) for the rFXIII Supplies.

(c) If either of the two lots of vialed Recombinant Factor XIII described in item 1(a) of **Exhibit I** fail stability specifications when tested by ZGEN or its subcontractors during routine stability testing in October or November 2004, NN shall be entitled to a credit for each lot that failed in the amount of fifty thousand United States dollars (U.S. $50,000) against the first future milestone fee payable to ZGEN following such testing. If it is determined that any materials described in items 1(b) and (c) of **Exhibit I** did not meet the release

specifications as filed with the FDA or as set forth in the Avecia Agreement, as applicable, in effect at the time of release or were not stored properly prior to the Effective Date such that they cannot be used for their expected purposes in research and development, NN shall be entitled to a credit against the first future milestone fee payable to ZGEN following such determination equal in amount to (i) the weight of such materials divided by the aggregate weight of all materials in items 1(b) and (c) of **Exhibit I** (ii) multiplied by five hundred sixty-seven thousand United States dollars (U.S. $567,000). For the avoidance of doubt, the aggregate of all amounts that may be creditable pursuant to this **Section 5.5(c)** against future milestone fees due pursuant to **Section 4.2** shall not exceed six hundred sixty-seven thousand United States dollars (U.S. $667,000).

(d) For each GMP manufacturing run by Avecia described in items 2 and 3 of **Exhibit I** (a **"GMP Manufacturing Run"**), ZGEN and NN will, within sixty (60) days after notification from Avecia that its batch records are ready for review, perform a joint quality audit of such batch records to determine whether the GMP Manufacturing Run meets the release specifications set forth in the Avecia Agreement (according to assays performed by ZGEN or Avecia as relied upon by ZGEN). During such sixty (60) day period, ZGEN and NN will perform joint audits of Avecia's manufacturing facility and quality system in regard to manufacturing and release testing and the facility and quality systems of any ZGEN subcontractors (to the extent permitted by ZGEN's contracts) in regard to release testing of any drug substance. During such sixty (60) day period, NN will also audit ZGEN's facility and quality systems in regards to release testing of any drug substance. Within sixty (60) days after completion of such audits, NN will determine and inform ZGEN whether the GMP Manufacturing Run was prepared in accordance with NN's standards for cGMP, provided that any major nonconformances have been resolved to NN's satisfaction. Following the completion by ZGEN or its subcontractors of the validation of assays for release of Factor XIII drug substance pursuant to **Section 5.3**, ZGEN or its subcontractors will test each GMP Manufacturing Run using these validated assays and will provide a certificate of analysis to NN for each GMP Manufacturing Run based upon these validated assays. For each GMP Manufacturing Run that NN has determined was not prepared in accordance with cGMP (i.e., determined within sixty (60) days after completion of the audits and within thirty (30) days after receiving the certificate of analysis from ZGEN), NN shall be entitled to a credit of eight hundred thousand United States dollars (U.S. $800,000) against the first future milestone fee payable to ZGEN following NN's determination. For the avoidance of doubt, the aggregate of all amounts that may be creditable pursuant to this **Section 5.5(d)** against future milestone fees due pursuant to **Section 4.2** shall not exceed one million six hundred thousand United States dollars (U.S. $1,600,000); provided, however, that in the event NN uses any GMP Manufacturing Run material, NN shall not be entitled to a credit pursuant to this **Section 5.5(d)** and if NN has taken a credit for such material, NN shall pay to ZGEN the amount of such credit.

(e) Except as provided in **Section 5.2**, each Party shall be responsible for its own costs of performing any testing and quality audit on any GMP Manufacturing Run material, including facility audits.

(f) It is acknowledged by the Parties that any failure of GMP Manufacturing Run material to meet cGMP as determined by NN pursuant to **Section 5.5(d)**, shall constitute a CMC issue for the purposes of **Section 4.2(e)(iv)**.

(g) AT THE EFFECTIVE DATE, THE rFXIII SUPPLIES ARE BEING SOLD "AS IS" AND WITHOUT ANY REPRESENTATIONS OR WARRANTIES BY ZGEN, EXCEPT FOR A PASS-THROUGH OF THE WARRANTIES, AND RESPECTIVE LIMITATIONS, PROVIDED BY AVECIA. ZGEN MAKES NO REPRESENTATIONS OR WARRANTIES, EXPRESS OR IMPLIED, OF ANY TYPE WHATSOEVER, REGARDING THE rFXIII SUPPLIES, AND EXPRESSLY DISCLAIMS ANY IMPLIED WARRANTIES, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, SAMPLES PREVIOUSLY PROVIDED OR NONINFRINGEMENT.

Article 6
Development Reports and Records

Section 6.1. **Development Reports.** NN shall provide ZGEN written semiannual reports within one month after Novo's semiannual project review, on research and development progress and management approved plans for research and development for all Licensed Products by NN and each of its Affiliates and Sublicensees, including a description of and progress on significant preclinical, clinical and regulatory plans, projected time lines and actual events related to this Agreement, such as initiation and results of clinical trials and filing of significant regulatory documents. These reports shall contain the same level of the information and assessments (but not financial information) that is contained in Novo's internal, semiannual reports to Novo's senior management with respect to the Licensed Products. NN and each of its Affiliates and Sublicensees operating hereunder shall keep true, complete and accurate records for the purposes of showing their research, development and commercialization progress. ZGEN shall have the right to reasonably review and discuss with the project leader at Novo and any Sublicensees (other than Affiliates of NN) their respective research, development and commercialization plans, progress, results and efforts under this Agreement, *provided that* ZGEN has given reasonable advance notice to NN with respect to Novo and such Sublicensees and has not sought to contact them directly initially. NN shall cooperate with ZGEN's reasonable requests for information regarding such research, development and commercialization. The first such report shall be due no later than six (6) months after the Effective Date; subsequent reports shall be due every six (6) months thereafter until the First Commercial Sale of each Licensed Product for a particular indication under this Agreement in both the United States and European Union.

Section 6.2. **Dose Escalation Studies and CPOC Studies.** With respect to the Dose Escalation studies pursuant to **Section 3.3** and the CPOC Studies pursuant to **Section 3.4**, NN shall provide ZGEN with the final protocols for such studies (i.e., when forwarded to potential clinical trial sites) and reasonably discuss with ZGEN the final study reports (known as "Integrated Clinical Trial Reports") generated in accordance with Novo's internal guidelines for such studies. In addition, NN shall provide and reasonably discuss with ZGEN the reports generated in accordance with Novo's internal guidelines with respect to the Statistical Analysis and selection of the Phase III Development Candidate pursuant to **Sections 3.5** and **3.6**.

Section 6.3. **Preliminary Assessment.** As soon as NN has unblinded any of the Dose Escalation studies or CPOC Studies and performed a preliminary assessment of such studies or the Statistical Analysis, a representative of NN who is knowledgeable about the preliminary assessment shall call the senior clinical officer at ZGEN to discuss such preliminary assessment; *provided, however,* in the event NN will be making a public announcement of the preliminary assessment within a short time, ZGEN need not be advised of such preliminary assessment.

Section 6.4 **Confidentiality.** Any information provided to ZGEN under this **Article 6** shall be subject to the confidentiality provisions of **Article 10** and used by ZGEN solely for purposes of monitoring NN's progress and decisions regarding the research, development and commercialization of Licensed Products, unless the information must be provided to the licensor under the UW Agreement or Aventis Agreement (subject to the confidentiality provisions thereof), the information is no longer confidential pursuant to **Section 10.2** or otherwise specifically agreed in writing by the Parties.

Article 7
Patent Prosecution

Section 7.1. **Prosecution.** At its sole cost and expense, NN shall be solely responsible for the prosecution and maintenance, including prosecuting interferences and oppositions, of the Licensed Patents set forth in **Exhibit A** and the Sublicensed Patents set forth in **Exhibits C** and **D**. Upon NN's reasonable request and at no out-of-pocket expense to ZGEN, ZGEN shall render such reasonable assistance, execute any documents and do such other acts as may be reasonably necessary in connection with the prosecution or maintenance of any such

Licensed Patents and Sublicensed Patents by NN. To keep ZGEN apprised of its efforts, NN shall provide ZGEN promptly upon receipt with copies of all office actions and significant communications and correspondence from U.S. and foreign patent offices and foreign associates, and copies of NN's significant responses and amendments for all patent applications included in such Licensed Patents and Sublicensed Patents, including copies of newly filed related patent applications. ZGEN shall have the right to comment on and to discuss prosecution and maintenance activities with NN, and NN shall consider the same in good faith. The Parties will cooperate to ensure transfer of such prosecution and maintenance efforts to NN promptly following the Effective Date. In prosecuting and maintaining the Licensed Patents set forth in **Exhibit A** and the Sublicensed Patents set forth in **Exhibits C** and **D** under this **Section 7.1**, NN shall employ efforts that are no less than it uses for the prosecution and maintenance of its own patents and patent applications. At its sole cost, expense and discretion, ZGEN shall be solely responsible for the prosecution and maintenance, including prosecuting interferences and oppositions, of the Licensed Patents set forth in **Exhibit B**. ZGEN shall provide NN promptly upon receipt with copies of all office actions and significant communications and correspondence from U.S. and foreign patent offices and foreign associates, and copies of ZGEN's significant responses and amendments for all patent applications included in the Licensed Patents set forth in **Exhibit B.** NN shall have the right to comment on and to discuss prosecution and maintenance activities with ZGEN, and ZGEN shall consider the same in good faith. The prosecution and maintenance of the Sublicensed Patents set forth in **Exhibit E** shall be subject to the terms of the Aventis Agreement.

Section 7.2. **Abandonment.** NN, in its sole discretion, may elect to discontinue the prosecution and/or maintenance of any Licensed Patent set forth in **Exhibit A** or any Sublicensed Patent set forth in **Exhibits C** and **D**. Upon such election, NN shall so advise ZGEN in writing at least sixty (60) days in advance, and ZGEN shall have the right to continue such prosecution or maintenance at ZGEN's expense, in which event such patent or patent applications (and patents issuing thereon) shall be removed from the definition of Licensed Patent or Sublicensed Patent, as the case may be, and from the licenses or sublicenses granted hereunder. ZGEN, in its sole discretion, may elect to discontinue the prosecution and/or maintenance of any Licensed Patent set forth in **Exhibit B**. Upon such election by ZGEN, ZGEN shall so advise NN in writing at least sixty (60) days in advance and NN shall have the right, at its expense, to file an application to prosecute such Licensed Patent only as to claims specifically naming rFXIII and continue the prosecution thereof so long as such action does not jeopardize or adversely affect the rights of ZGEN's other licensees. With respect to maintaining any issued patents included in any Licensed Patent set forth in **Exhibit B**, NN shall have the right, together with ZGEN's other licensees of such patent, to maintain such patents at the expense of NN and the other licensees and with such other terms and arrangements as they may agree.

Section 7.3. **Patent Term Extension.** NN shall advise ZGEN of Marketing Approval by any Regulatory Agency to market any Licensed Product and of any other governmental approval obtained by or on behalf of NN, any Affiliate or Sublicensee that is pertinent to any patent term extension (including supplementary protection certificates) for any Licensed Patent or the Sublicensed Patent within ten (10) days after receiving such approval. NN, at its sole discretion and after notice to ZGEN, may seek a patent term extension for any Licensed Patent set forth in **Exhibit A** or Sublicensed Patent as set forth in **Exhibits C** and **D** after considering in good faith any input from ZGEN. Any patent term extension of a Licensed Patent set forth in **Exhibit B** shall only be made by ZGEN, in its sole discretion, after considering any input from NN and any other licensees. Any request for patent term extension of a Sublicensed Patent set forth in **Exhibit E** shall be subject to the terms of the Aventis Agreement. Unless the Parties agree otherwise, and except for the Sublicensed Patents set forth in **Exhibit E** and the Licensed Patents set forth in **Exhibit B**, all filings for such extension shall be made by NN at its sole cost and expense, and NN shall promptly reimburse ZGEN for its out-of-pocket costs related thereto. The Parties shall cooperate with any efforts to seek patent term extension, including diligently supplying all pertinent information pertaining to such patent term extension, and with all information and supporting documents required to comply with all laws pertaining to the extension of such patent term. With respect to the Sublicensed Patents set forth in **Exhibit E** controlled by Aventis, ZGEN will, at its cost and expense (but not with respect to any payments to Aventis), cooperate with NN in seeking the consent of Aventis to reasonably requested amendments to the Aventis Agreement.

Section 7.4. **Sublicensed Patents**. It is recognized that this **Article 7** is subject to the rights and obligations under, and compliance with the terms of, the UW Agreement and the Aventis Agreement.

Article 8
Patent Infringement

Section 8.1. **Notice of Infringement and Conference.** Each Party shall promptly inform the other Party in writing if it becomes aware of any alleged or threatened infringement of any Licensed Patents or Sublicensed Patents by a Third Party with respect to a Licensed Product. Upon receipt of such written notice, the Parties shall confer regarding all available evidence of infringement or attack, and the manner of addressing such infringement or attack. The Parties may agree to pursue the matter jointly.

Section 8.2. **NN Has First Right.** Unless the Parties agree otherwise, NN shall have the first right, but not the obligation, to initiate and control any infringement action, including cease and desist letters and lawsuits, at its expense, to enforce the Licensed Patents set forth in **Exhibits A** and **B** or the Sublicensed Patents set forth in **Exhibits C** and **D** against any infringer or alleged infringer of the such Licensed Patents or Sublicensed Patents to the extent exclusively licensed hereunder to NN. NN shall notify ZGEN of its decision whether to initiate such an infringement action, but in no event later than sixty (60) days after the conference described in **Section 8.1**, and before initiating such infringement action, NN shall consider in good faith the views of ZGEN presented in a timely manner following notification of NN's decision. NN shall keep ZGEN reasonably apprised of the progress of the matter. If ZGEN has agreed to join the action at the request of NN or has been made an involuntary plaintiff (or defendant) in the action and NN's legal counsel is unable to represent ZGEN because of a *bona fide* conflict of interest, ZGEN may engage other competent legal counsel (but only one firm) to represent ZGEN in any such suit or legal proceeding and NN shall reimburse ZGEN for the reasonable fees and expenses of such counsel. If ZGEN does not wish to be represented by NN's legal counsel for reasons other than a *bona fide* conflict of interest, then ZGEN may engage competent legal counsel of its own choosing to represent it at its own expense. NN shall indemnify, defend and hold harmless the Indemnitees (as defined in **Section 12.1**) from any and all claims, counterclaims, damages, judgments, costs, expenses (including attorneys' fees), liability and obligations directly associated with any claim or legal proceedings instituted by NN under this **Section 8.2**. Any infringement action with respect to the Sublicensed Patents set forth in **Exhibit E** shall be subject to the terms of the Aventis Agreement.

Section 8.3. **Awards.** Any recovery by NN in proceedings instituted by NN pursuant to **Section 8.2** shall first be used to reimburse NN for its reasonable out-of-pocket costs and legal fees incurred to conduct such proceedings, including its reimbursement, if any, of ZGEN's costs and legal fees pursuant to this **Article 8**. Any remaining amount shall be divided as follows: NN-[70]%; ZGEN-[30]%.

Section 8.4. **Settlement.** NN may enter into any settlement, consent judgment or other voluntary final disposition of any proceeding under **Section 8.2** without ZGEN's prior written consent so long as the Licensed Patents and Sublicensed Patents would not be adversely affected, such settlement is not otherwise inconsistent with the terms of this Agreement and ZGEN receives a general release of any claims against it in such proceeding and ZGEN is promptly provided thereafter a copy of such settlement, consent judgment or other voluntary disposition. Any other settlement, consent judgment or voluntary final disposition of any proceeding under **Section 8.2** by NN shall require the prior written consent of ZGEN, which consent shall not be unreasonably withheld or delayed. Any recovery by NN in connection with such settlement, consent judgment or other voluntary final disposition shall be applied first to reimburse NN for its reasonable out-of pocket costs and legal fees incurred and any remaining amount shall be divided as follows: NN-[70]%; ZGEN-[30]%; *provided, however,* that noncash consideration or compensation received or to be received by NN shall be valued at a fair market value and ZGEN's share (as provided herein) paid to ZGEN in cash by NN and, *provided further* that any dispute between the Parties regarding such fair market value shall be established by binding arbitration in New York, New York and conducted in accordance with the Non-Administered Arbitration Rules & Commentary (Rev. 2000) of the CPR Institute for Dispute Resolution before one independent and impartial arbitrator who has

training and experience as a mediator of pharmaceutical industrial licensing and other general commercial matters.

Section 8.5. **ZGEN Has Secondary Right.** If NN has not taken any action pursuant to **Section 8.2** to stop such infringement within sixty (60) days after the conference described in **Section 8.1** or desires to cease to continue any such action to stop such infringement (as to which NN shall provide a reasonable notice to ZGEN prior to discontinuing an infringement proceeding) and such infringement (and continued infringement) would be materially detrimental to the development/commercialization of any Licensed Product hereunder, or has resulted in sales of excess of seventy-five million United States dollars (U.S. $75,000,000) in the aggregate, ZGEN shall, at its sole discretion, have the right, but not the obligation, to take legal action regarding such infringement (including continuing NN's infringement proceeding in the name of ZGEN), as ZGEN deems necessary and desirable at its expense. In the event of any continuance by ZGEN of an NN infringement action, NN shall reasonably cooperate, at no out-of-pocket expense to NN, in all actions reasonably necessary to transfer control of the proceedings from NN to ZGEN. If NN is made an involuntary plaintiff (or defendant) in the action and ZGEN's legal counsel is unable to represent NN because of a *bona fide* conflict of interest, NN may engage other competent counsel (but only one firm) to represent NN in such action and ZGEN shall reimburse NN for the reasonable fees and expenses of such counsel. ZGEN may enter into any settlement, consent judgment or other voluntary final disposition of any proceeding under this **Section 8.5** without NN's prior written consent so long as the Licensed Patents and Sublicensed Patents would not be adversely affected, such settlement is not otherwise inconsistent with the terms of this Agreement and NN receives a general release of any claims against it in such proceeding, and NN is promptly provided thereafter a copy of such settlement, consent judgment or other voluntary disposition. Any other settlement, consent judgment or voluntary final disposition of any proceeding under this **Section 8.5** by ZGEN shall require the prior written consent of NN, which consent shall not be unreasonably withheld or delayed. Any recovery by ZGEN in proceedings instituted by ZGEN pursuant to this **Section 8.5** and any recovery pursuant to any settlement, consent judgment or other voluntary disposition thereof shall first be used to reimburse ZGEN for its reasonable out-of-pocket costs and legal fees incurred and any remaining amount shall be divided as follows: ZGEN-70%; .NN-30%; *provided, however*, that noncash consideration or compensation received or to be received by ZGEN shall be valued at a fair market value and NN's share (as provided herein) paid to NN in cash by ZGEN and, *provided further* that any dispute between the Parties regarding such fair market value shall be established by binding arbitration in accordance with the procedure set forth in the last proviso of **Section 8.4**.

Section 8.6. **Cooperation.** In any legal proceeding conducted under this **Article 8**, each Party shall, without charge (except for the reimbursement of its out-of-pocket costs), render such reasonable assistance, execute any documents and do such other as may be reasonably necessary in such legal action as the other Party may reasonably request. Each Party shall keep the other Party reasonably informed as to the progress of any proceedings hereunder.

Section 8.7 **Affiliates and Sublicensees.** NN shall require its Affiliates and Sublicensees to comply with this **Article 8**.

Section 8.8. **Sublicensed Patents.** It is recognized that this **Article 8** is subject to the rights and obligations under, and compliance with the terms of, the UW Agreement and the Aventis Agreement.

Article 9
Term and Termination

Section 9.1. **Term and Expiration.** This Agreement and the licenses contained herein shall come into force on the Effective Date. Unless terminated earlier, the licenses provided hereunder for any Licensed Products shall expire on the date on which ZGEN is no longer entitled to receive a royalty with respect thereto, and this Agreement shall expire on the date on which ZGEN is no longer entitled to receive a royalty from NN on any Licensed Product under this Agreement. After expiration (but not termination), NN shall have a fully paid-up

(except for payments to third parties), irrevocable, nonexclusive license under the Licensed Know-How to make, have made, use, sell and have sold Know-How Products.

Section 9.2. **Termination by NN for Avoidance of Annual Fee.** NN may terminate this Agreement in accordance with the provisions of **Section 4.10**.

Section 9.3. **Insolvency.** Either Party shall have the right to terminate this Agreement by written notice to the other Party (a) if the other Party is declared insolvent or bankrupt by a court of competent jurisdiction, (b) if a voluntary or involuntary petition in bankruptcy is filed in any court of competent jurisdiction against the other Party and such petition remains undismissed, undischarged or unbonded for a period of ninety (90) days after the filing thereof, or (c) if the other Party shall make or execute an assignment for the benefit of creditors generally, have a receiver, administrator or an equivalent official appointed with respect to its properties or undertakings, enter into any liquidation or become insolvent. In the event of ZGEN's bankruptcy (particularly where associated with ZGEN's breach of its obligations under this Agreement) and NN's failure to elect termination under this **Section 9.3**, all rights and licenses granted under this Agreement by ZGEN to NN, to the maximum extent permitted by law, shall be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code, 11 U.S.C. § 101, *et seq.*, licenses of rights to "intellectual property" as defined under Section 101 (35A) of the United States Bankruptcy Code. The Parties agree that NN shall retain and may fully exercise all of its rights and elections under the United States Bankruptcy Code in the event of a bankruptcy by ZGEN. The Parties further agree that in the event of the commencement of a bankruptcy proceeding by or against ZGEN under the United States Bankruptcy Code, NN may seek access to any such intellectual property pertaining to the rights granted by ZGEN in the licenses hereunder.

Section 9.4. **Breach.** Each Party shall have the right to terminate this Agreement after written notice to the other Party in the event the other Party is in material breach of this Agreement, unless the other Party cures such breach within sixty (60) days (or in the event such breach is a failure to pay, thirty (30) days) after the date of notice; *provided, however*, that any termination shall not release either Party from any obligations accrued prior thereto.

Section 9.5. **Termination of License With Respect to Contested Patent Rights.** To the extent NN or its Affiliate or Sublicensee, or any entity acting in concert with or on behalf of any of them, commences any action or asserts any formal position in any forum (including a court, patent office or an arbitral tribunal, and whether in the form of petitions for declaratory relief, claims, counterclaims, defenses, interferences, petitions for re-examination, oppositions or otherwise) that any Licensed Patent or Sublicensed Patent is invalid or unenforceable, ZGEN may, at its option, remove such Licensed Patent or Sublicensed Patent, including any divisional, continuation (in whole or in part), foreign counterpart, reissue, reexamination, renewal or extension thereof and any patents issuing thereon, from the definition of Licensed Patents or Sublicensed Patents hereunder.

Section 9.6. **Effect of Expiration or Termination.** Expiration or termination of this Agreement shall not relieve the Parties of any obligations accruing prior to such expiration or termination. In addition to any provision of this Agreement that expressly provides for its survival, any accrued obligation and the provisions of **Article 1, Section 2.3** (second sentence), **Section 4.11, Article 6, Section 8.2** (next to last sentence addressing indemnification), **Section 8.3, Section 8.4, Section 8.6, Section 9.1** (last sentence in the event of expiration), **Section 9.6, Section 9.8, Section 9.9, Article 10, Section 11.5, Article 12** and **Article 13** shall survive the expiration or termination of this Agreement. Expiration or termination of this Agreement shall not affect a Party's ability to seek any other remedies available at law.

Section 9.7. **Termination of Licenses.** Upon termination of this Agreement, all licenses granted hereunder shall terminate.

Section 9.8. **Return of Patent Prosecution.** Upon termination of this Agreement, NN shall take all necessary steps to transfer to ZGEN all documents reasonably necessary for ZGEN to maintain and prosecute the

Licensed Patents set forth in **Exhibit A** and Sublicensed Patents set forth in **Exhibits C** and **D**, including prosecuting interferences and oppositions. The Parties will cooperate to ensure transfer of such prosecution and maintenance efforts to ZGEN promptly following the termination date. Any subsequent office actions, communications, correspondence or other information received by NN related to the Licensed Patents or such Sublicensed Patents shall be promptly forwarded to ZGEN when received.

Section 9.9. **Return of Information and Assignments.** Upon termination (but not expiration) of this Agreement, NN shall (a) cause all materials containing any Licensed Know-How (including the information, documents, files and materials transferred pursuant to **Article 5**) to be delivered to ZGEN within six (6) months, (b) at ZGEN's election, terminate (or assign to ZGEN, to the extent assignable) to the extent related to rFXIII, the nonexclusive license received by NN under the WRF Agreement pursuant to **Section 2.4** and (c) at ZGEN's election, assign and transfer to ZGEN all rights in any regulatory filings transferred to NN pursuant to **Section 2.6** and requested by ZGEN, and cause each of its Affiliates and Sublicensees to take such actions. In addition, if termination is due to a material breach of this Agreement by NN under **Section 9.4** or the insolvency of NN under **Section 9.3**, NN shall (i) at ZGEN's election, assign to ZGEN all rights in any preclinical and/or clinical data, clinical trial protocols, regulatory applications or approvals (e.g., INDs) (to the extent assignable) requested by ZGEN, and cause each of its Affiliates and Sublicensees to take such actions, and thereafter ZGEN shall be responsible for all future costs and charges related thereto that thereafter accrue and (ii) during the six (6) months following termination, discuss with ZGEN information and data that exists with respect to rFXIII and Licensed Products and provide to ZGEN such relevant information and data requested by ZGEN, which it may thereafter use, either alone or with others. For the avoidance of doubt, in no event shall ZGEN receive any rights or materials under this **Section 9.9** with respect to rFVIIa or Combination rFVIIa/rFXIII.

Article 10
Confidentiality

Section 10.1. **Confidentiality Obligation.** Except as otherwise authorized under this Agreement, during the term of this Agreement and for a period of five (5) years thereafter or ten (10) years after the Effective Date, whichever is longer, each Party and Novo shall maintain as secret and confidential all Confidential Information obtained from the other Party or Novo pursuant to this Agreement or prior to and in contemplation of this Agreement, and all other Confidential Information that it may acquire from the other Party or Novo in the course of this Agreement. Each Party and Novo shall respect the proprietary rights of the other Party or Novo in such Confidential Information, use the same exclusively for the purposes of this Agreement, and disclose the same only to those of its representatives to whom and to the extent that such disclosure is reasonably necessary for the purposes of this Agreement. The obligations under this **Section 10.1** shall survive the termination of this Agreement.

Section 10.2. **Release from Confidentiality Obligation.** Notwithstanding the provisions of **Section 10.1**, a Party shall be permitted to disclose any Confidential Information of the other Party to its patent practitioners or any patent office in any country, as is reasonably required for filing or prosecuting any patent application permitted to be filed by it hereunder. Furthermore, the obligations of **Section 10.1** shall not apply to Confidential Information that:

(a) was properly in the possession of the receiving Party or Novo, without any restriction on use or disclosure, prior to receipt from the disclosing Party or Novo, and such possession can be demonstrated by competent evidence of the receiving Party or Novo;

(b) is in the public domain by public use, publication, general knowledge or the like, or after disclosure hereunder becomes general or public knowledge through no fault of the receiving Party or Novo;

(c) is properly obtained by the receiving Party or Novo from a Third Party not under a confidentiality obligation;

(d) is independently developed by or on behalf of the receiving Party or Novo without the assistance of the Confidential Information of the disclosing Party or Novo; or

(e) is required to be disclosed by order of any court or governmental or regulatory authority after notification to the disclosing Party or Novo of the necessity to allow the disclosing Party or Novo to seek protection for the Confidential Information of the disclosing Party or Novo from such court or governmental or regulatory authority.

Section 10.3. Disclosure of Agreement. The Parties acknowledge that ZGEN may be obligated to file a copy of this Agreement with the U.S. Securities and Exchange Commission; *provided however*, that ZGEN shall request confidential treatment of any trade secrets or commercially sensitive items hereof to the extent such confidential treatment is reasonably available to it under the circumstances then prevailing. In the event of such filing, ZGEN shall provide NN, at least ten (10) days in advance of filing with the U.S. Securities and Exchange Commission, with an advance copy of this Agreement marked to show provisions for which ZGEN intends to seek confidential treatment and ZGEN shall reasonably consider NN's timely comments thereon.

Article 11
Representations, Warranties and Disclaimers

Section 11.1. Representations and Warranties. Each Party and Novo hereby represents and warrants to the other Party and Novo, as of the Effective Date, as follows:

(a) It is a corporation duly organized, and validly existing (and, in the case of ZGEN only, in corporate good standing) under the laws of the jurisdiction in which it is incorporated;

(b) It has the corporate and legal right, title, authority and power to enter into this Agreement;

(c) It has taken all necessary action to authorize the execution, delivery and performance of this Agreement;

(d) Upon the execution and delivery of this Agreement, this Agreement shall constitute a valid and binding obligation of it, enforceable in accordance with its terms, except as enforceability may be limited by applicable bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' and contracting parties' rights generally and except as enforceability may be subject to general principles of equity (regardless of whether such enforceability is considered in a proceeding in equity or at law);

(e) The performance of its obligations under this Agreement will not conflict with or result in the breach of any agreements, contracts or other arrangements to which it is a party; and

(f) It will not during the term of this Agreement enter into any agreements, contracts or other arrangements that would prevent it from meeting its obligations or adversely impact the other Party's rights under this Agreement.

Section 11.2. Further Representations and Warranties of ZGEN. ZGEN hereby represents and warrants to NN as follows:

(a) ZGEN will comply with all applicable laws, regulations and guidelines in connection with the performance of ZGEN's obligations under this Agreement;

(b) As of the Effective Date and except as described in the letter to NN from ZGEN dated October 4, 2004, ZGEN is the joint or exclusive owner of the Licensed Patents and, to the Best of its Knowledge, the exclusive licensee of the Sublicensed Patents for purposes of Recombinant Factor XIII, it has the full right and

power to grant the licenses and sublicenses set forth herein and there are no outstanding agreements, assignments or encumbrances with respect to the Licensed Patents or, to the Best of its Knowledge, Sublicensed Patents inconsistent with the provisions of this Agreement;

(c) As of the Effective Date, each of the patents set forth in **Exhibits A, B** and **C**, and to the Best of its Knowledge, **Exhibits D** and **E**, has been duly maintained;

(d) As of the Effective Date, none of the patents or patent applications set forth in **Exhibits A, B, C, D** and **E** (i) is subject to a pending interference action, opposition action, reexamination proceeding, litigation or other similar action by a Third Party challenging such patents or patent applications, other than actions by patent offices in connection with the prosecution of patent applications or as otherwise described in the letter to NN from ZGEN dated October 4, 2004, (ii) has been abandoned, (iii) has been asserted to be invalid or unenforceable in a written communication to ZGEN or (iv) is the subject of an on-going infringement by others with respect to Recombinant Factor XIII; *provided, however,* that the representations and warranties made by ZGEN in the foregoing clauses (i) and (ii) with respect to **Exhibits C, D and E**, and in the foregoing clause (iv) with respect to **Exhibits A, B, C, D and E**, are made to the Best of its Knowledge;

(e) As of the Effective Date, each of the Aventis Agreement, UW Agreement and WRF Agreement is in full force and effect, true and complete copies thereof have been provided to NN and no event has occurred which (by the giving of notice or the passing of time or both) would (i) constitute a material breach or default by ZGEN or, to the Best of its Knowledge, another party, (ii) permit termination by ZGEN or, to the Best of its Knowledge, another party or (iii) result in ZGEN's loss of exclusivity under any such agreement;

(f) As of the Effective Date, ZGEN has paid the yearly amounts due under the WRF Agreement to maintain the WRF Option, which has not been exercised or terminated;

(g) As of the Effective Date and except for the patents and patent applications identified in a letter to NN from ZGEN dated October 4, 2004, **Exhibits A, B, C, D** and **E** identify all of the pending patent applications and unexpired patents that are owned or Controlled by ZGEN that contain one or more claims specifically naming rFXIII and claiming (i) rFXIII as a composition of matter, (ii) a process, formulation and/or mixture comprising rFXIII, (iii) a method of making or manufacturing rFXIII, or (iv) a method of using rFXIII; and

(h) As of the Effective Date, copies of all regulatory filings, approvals and orphan drug designation listed in **Exhibit G** (but not including material incorporated by reference that predates September 26, 2001) and, to the Best of its Knowledge, copies of all written communications (or minutes, where available, of oral communications) with Regulatory Agencies after September 26, 2001 regarding such filings, approvals and designation have been supplied or made available to NN.

Section 11.3. **Further Representations and Warranties of NN.** NN hereby represents and warrants to ZGEN that NN will comply with all applicable laws, regulations and guidelines in connection with the exercise of NN's license rights under this Agreement.

Section 11.4. **Warranty Disclaimer.** EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT, NEITHER PARTY NOR NOVO MAKES ANY WARRANTY WITH RESPECT TO rFXIII, LICENSED PRODUCTS, LICENSED PATENTS, SUBLICENSED PATENTS, LICENSED KNOW-HOW (INCLUDING THE INFORMATION, DOCUMENTS, FILES AND MATERIALS TRANSFERRED PURSUANT TO **ARTICLE 5**) OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND EACH PARTY AND NOVO HEREBY DISCLAIMS WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, SAMPLES PREVIOUSLY PROVIDED, NONINFRINGEMENT AND PATENTABILITY WITH RESPECT TO ANY AND ALL OF THE FOREGOING.

Section 11.5. **Limited Liability.** EXCEPT IN THE CASE OF GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, NONE OF NOVO, NN OR ZGEN WILL BE LIABLE WITH RESPECT TO ANY MATTER ARISING UNDER THIS AGREEMENT UNDER ANY CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY FOR ANY PUNITIVE OR EXEMPLARY DAMAGES.

Article 12
Indemnification

Section 12.1. **Personal Injury or Property Damage.** NN shall indemnify, defend and hold harmless ZGEN and its directors, officers, employees and agents (collectively, the "**Indemnitees**") from and against any and all claims, judgments, costs, awards, expenses (including, but not limited to, any attorneys' fees) or liability of any kind arising out of personal injury or property damage caused or alleged to be caused by any Licensed Product developed, manufactured, used or sold by NN or any of its Affiliates or Sublicensees or the use of any ZGEN IP or Sublicensed Patents by NN or any of its Affiliates or Sublicensees. In addition, NN shall assume all obligations for warranties and product liability claims that accompany or result from the sale or use of any Licensed Product developed, manufactured or sold by NN or any of its Affiliates or Sublicensees and shall indemnify, defend and hold harmless the Indemnitees from and against any and all claims, judgments, costs, awards, expenses (including, but not limited to, any attorneys' fees) or liability of any kind arising from a customer's or user's use of any Licensed Product developed, manufactured or sold by NN or any of its Affiliates or Sublicensees and relating to such warranty obligations or product liability claims. NN's obligations under this **Section 12.1** shall not apply to any Indemnitee to the extent that such Indemnitee is grossly negligent or engaged in willful misconduct. ZGEN shall (a) promptly notify NN of any claim, judgment, cost, award or expense covered by this **Section 12.1**, (b) reasonably cooperate with NN in the defense of such claim, judgment, cost, award or expense, at NN's cost and expense in connection therewith, (c) allow NN to control the defense of the claim, judgment, cost, award or expense, including the taking of any action necessary to permit NN to control such defense, and, (d) not compromise or settle the claim, judgment, cost, award or expense without NN's prior written consent, which consent shall not be unreasonably withheld.

Section 12.2. **Patent Infringement.** NN shall indemnify, defend and hold harmless the Indemnitees from and against any and all claims, judgments, costs, awards, expenses (including, but not limited to, any attorneys' fees) or liability of any kind arising out of or connected with the actual or alleged infringement or misappropriation of any patent or other proprietary right of any Third Party by reason of NN or its Affiliates or Sublicensees having made, imported, used, sold or offered for sale any Licensed Product; *provided, however*, that in the event a suit, claim or action is brought against NN by a Third Party, ZGEN shall render reasonable assistance to NN upon request of NN, at NN's cost and expense in connection therewith. NN's obligations under this **Section 12.2** shall not apply to any Indemnitee to the extent that such Indemnitee is grossly negligent or engaged in willful misconduct.

Section 12.3. **Insurance.** NN shall maintain and cause its Affiliates and Sublicensees to maintain appropriate product liability insurance with respect to the development, manufacture and sale of Licensed Products in such amount as NN customarily maintains with respect to sales of its other products. NN shall maintain and cause its Affiliates and Sublicensees to maintain such insurance for so long as it continues to manufacture or sell Licensed Products, and thereafter for so long as NN customarily maintains insurance with respect to sales of its other products.

Article 13
Miscellaneous

Section 13.1. **Assignment.** This Agreement may not be assigned by either Party without the prior written consent of the other Party except to an Affiliate of a Party or to a successor or a purchaser of all or substantially all of the assets of a Party and its Affiliates related to the hemostasis field; *provided, however*, that in the event of an assignment by NN to an Affiliate, the Affiliate's rights under this Agreement shall terminate once

it ceases being an "**Affiliate**" of Novo (however, its rights may be reassigned back to Novo at the time it ceases being an "**Affiliate**" of Novo), and *provided further*, that any transfer of NN or substantially all of its assets to other than a successor or a purchaser of all or substantially all of Novo's assets and business, without the prior written consent of ZGEN, shall be deemed to be a prohibited assignment of this Agreement and material breach of this Agreement, and *provided further*, any transfer, direct or indirect, of control of NN such that it is no longer an Affiliate of Novo, shall be deemed to be a prohibited assignment hereunder and a material breach of this Agreement. If, as a result of any assignment of any rights or interest in this Agreement by NN, any payment by or on behalf of NN to ZGEN is subject to an increased level of tax withholding than would have been the case under this Agreement with payments by NN from Denmark/Switzerland, and ZGEN cannot use any related tax credit as an offset against its obligation to pay United States federal income tax in the Calendar Year in which the withholding is effected, then NN shall pay ZGEN an amount such that, after deduction of any amount required to be withheld, ZGEN receives the same amount that it would have received but for the assignment. In the event of any permissible assignment under this Agreement, the assignor and assignee shall be jointly and severally liable for assignor's obligations hereunder. The assigning Party shall give the other Party prompt written notice of such assignment and obtain the agreement of the assignee to abide by the terms of this Agreement and to assume all of the assignor's obligations under this Agreement. ZGEN shall have the right to assign its right to receive any payments under this Agreement without NN's consent; *provided however*, that the assignee of such payments shall not have a right to any development information related to Licensed Products (other than the achievement of Event Milestones) and shall have no rights to Net Sales reports or access to information resulting from inspection/audit of records pertaining to Net Sales under **Section 4.11** if such assignee of the payments is a pharmaceutical or biotechnology company and, *provided further*, such assignee shall be subject to the confidentiality obligations of **Article 10**. Novo may not transfer or assign its obligations under **Section 13.20(b).**

Section 13.2. **Relationship between the Parties.** Nothing in this Agreement is intended to create or shall be deemed to constitute a partnership, agency or joint venture relationship between the Parties or Novo or their Sublicensees, contractors or licensees. Neither Party shall be responsible for the acts or omissions of the other Party, and neither ZGEN nor Novo shall be responsible for the acts or omissions of the other. Neither Party nor Novo shall have the authority to speak for, represent or obligate the other Party or Novo in any way without the prior written authority of the other Party or Novo, as the case may be.

Section 13.3. **Public Announcements.** Except as otherwise may be required by law or regulation, neither Party nor Novo shall make any public announcement, written or oral, concerning this Agreement or the subject matter hereof, without the prior written approval of the other Party or Novo, as the case may be, such approval not to be unreasonably withheld or delayed. However, ZGEN shall have the right to disclose or announce information concerning the existence and general nature of this Agreement, *provided that* disclosure of any Confidential Information shall only be made under an obligation or expectation of confidentiality.

Section 13.4. **Use of Names, Trade Names and Trademarks.** Except as provided herein, nothing contained in this Agreement shall be construed as conferring any right on either Party or Novo to use in advertising, publicity or other promotional activities any name, trade name, trademark or other designation of the other Party or Novo, including any contraction, abbreviation or simulation of any of the foregoing, unless the express written permission of such other Party or Novo has been obtained.

Section 13.5. ***Force Majeure.*** If either Party or Novo is prevented or delayed in the performance of any of its obligations under this Agreement by *force majeure*, and if such Party or Novo gives written notice thereof to the other Party (or Parties in the case of Novo) specifying the matters constituting *force majeure*, together with such evidence as it can reasonably give and specifying the period for which it is estimated that such prevention or delay will continue, then the Party in question or Novo, as the case may be, shall be excused from the performance of its obligations or the punctual performance thereof as the case may be as from the date of such notice for so long as such cause of prevention or delay shall continue. For the purpose of this Agreement, "***force majeure***" shall be deemed to be any cause affecting the performance of this Agreement arising from or

attributable to acts, events, omissions or accidents beyond the reasonable control of the Party or Novo, as the case may be.

Section 13.6. **Governing Law.** This Agreement shall be governed in all respects by the laws of the State of New York (without regard to its choice of law provisions). The UN Convention on Contracts for the International Sale of Goods shall not apply to this Agreement.

Section 13.7 **Submission to Jurisdiction**. Any suit, action or proceeding seeking to enforce any provision of, or based on any matter arising out of or in connection with, this Agreement or the transactions contemplated hereby shall be brought in the United States District Court for the Southern District of New York or any New York state court sitting in the County of New York, and each of the Parties and Novo hereby irrevocably consents to the jurisdiction of such courts (and of the appropriate appellate courts therefrom) in any such suit, action or proceeding and irrevocably waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of the venue of any such suit, action or proceeding in any such court or that any such suit, action or proceeding brought in any such court has been brought in an inconvenient forum. Process in any such suit, action or proceeding may be served on any Party or Novo anywhere in the world, whether within or without the jurisdiction of any such court. Without limiting the foregoing, each Party and Novo agrees that service of process on such Party or Novo as provided in this **Section 13.7** shall be deemed effective service of process on such Party or Novo.

Section 13.8 **WAIVER OF JURY TRIAL.** EACH OF THE PARTIES HERETO AND NOVO HEREBY IRREVOCABLY WAIVES ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.

Section 13.9. **Waiver of Remedies.** No forbearance, delay or indulgence by either Party in enforcing the provisions of this Agreement shall prejudice or restrict the rights of that Party, nor shall any waiver of its rights operate as a waiver of any subsequent breach, and no right, power or remedy herein conferred upon or reserved for either Party is exclusive of any other rights, power or remedy available to that Party.

Section 13.10. **Entire Agreement.** This Agreement and the Exhibits hereto constitute the entire agreement among the Parties and Novo and supersede all prior oral and written agreements, understandings or arrangements relating to the subject matter hereof, including all term sheets and the Mutual Confidential Disclosure Agreements between ZGEN and Novo dated September 26, 2002 and May 21, 2003, as amended. All information disclosed under such Mutual Confidential Disclosure Agreements that is Confidential Information shall be kept confidential in accordance with the terms of **Article 10** hereof. No addition to or modification of any provision of this Agreement shall be binding upon the Parties, unless made in writing and signed by a duly authorized representative of each of the Parties.

Section 13.11. **Notices.** All notices or other communication hereunder shall be in writing and in the English language and shall be deemed to have been duly given if delivered personally, faxed with receipt acknowledged (and with a confirmation copy also sent by registered mail, return receipt requested) or delivered by a recognized commercial courier service with receipt acknowledged, postage prepaid, as follows:

If to NN or Novo: Novo Nordisk Health Care AG
Andreasstrasse 15
8050 Zürich
Switzerland
Fax: +41 43 222 4404
Attention: General Manager

Novo Nordisk A/S
Novo Allé
DK-2880
Bagsvaerd
Denmark
Fax: +45 44 42 72 80
Attention: Chief Scientific Officer & Executive Vice President, Research & Development

Novo Nordisk Legal Department
Novo Allé
DK-2880 Bagsvaerd
Denmark
Fax: +45 4498 0670

If to ZGEN:

Development Reports Under Section 6.1

ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102
Fax: (206) 442- 6793
Attention: Senior Vice President & Chief Medical Officer

Royalty Reports under Section 4.11

ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102
Fax: (206) 442-6628
Attention: Controller

All other notices
ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102
Fax: 206-442-6678
Attention: Senior Vice President, Intellectual Property and Legal Affairs

or to such other addresses as the addressee may have specified in a notice duly given to the sender as provided herein. Such notices or other communication will be deemed effective as of the date so delivered (either personally or by courier service) or faxed.

Section 13.12. Severability. If any provision of this Agreement shall for any reason be held to be invalid or unenforceable, such provision shall be enforced to the maximum extent permitted by law and the fundamental intentions of the Parties and Novo hereunder, and the remaining provisions hereof shall not be affected, impaired or invalidated and shall continue in full force and effect.

Section 13.13. Headings. The headings contained herein are for reference only and shall not be considered a part of this Agreement, nor shall they in any way affect the interpretation hereof.

Section 13.14. Review of Agreement. This Agreement has been submitted to the scrutiny of both Parties, Novo and their counsel and shall be given a fair and reasonable interpretation in accordance with the

words hereof, without consideration or weight being given to its being drafted by or for one of the Parties or Novo.

Section 13.15. Compliance with Laws; Export Regulations. In the performance of this Agreement, each Party and Novo shall comply with all laws, regulations, rules, orders and other requirements, now or hereafter in effect, of any governmental authorities having jurisdiction. This Agreement and any information related to Licensed Know-How provided hereunder are subject to restrictions concerning the export of information and materials that may be imposed by a government. Accordingly, NN and Novo agree that it will not export, directly or indirectly, any information or materials acquired under this Agreement or any products utilizing such information or materials to any country for which a government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate agency of the government when required by an applicable statute or regulation.

Section 13.16. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

Section 13.17. Patent Marking. NN shall mark all Licensed Products with a legible notice indicating that the Licensed Products are covered by claims in a pending patent application or an issued patent included in the Licensed Patents or Sublicensed Patents.

Section 13.18. Data Retention/Documentation. Each Party and Novo, at its own costs, shall be responsible for archiving all relevant and required original documentation and raw data in relation to the research, development, manufacturing and control of the drug substance and drug product, including, with respect to NN, all documentation and data which has been provided to NN by ZGEN in original form and ZGEN shall not be required to maintain any copies thereof. All original notebooks shall be kept indefinitely by the Parties and Novo and development documentation shall be archived by the Parties and Novo in accordance with their documentation control policies, which shall comply with applicable law. All original documentation related to manufacturing shall be kept for the shelf life of the drug substance and drug products plus one year. It is acknowledged that it is ZGEN's intent to provide NN all original documentation that it has with respect to research, development, manufacture and control of drug substance and drug product, except original lab notebooks, copies of which will be provided to NN; *provided, however*, that any original documentation relating to manufacture and control of drug substance and drug product that ZGEN does not provide to NN shall be archived indefinitely. In case ZGEN desires to discard the data and documentation relating to manufacture and control of drug substance or drug product or the original notebooks ZGEN shall notify NN of such decision and NN may take over the responsibility for the archiving thereof at NN's cost.

Section 13.19. Pre-Approval Inspections. Upon reasonable advanced notice and during normal business hours, ZGEN shall allow any applicable health authority or Regulatory Agency to inspect ZGEN and to conduct reviews of any original documents or reports or any facilities that are deemed by the authority or Regulatory Agency to be related to the approval of a Factor XIII Product or a Combination Product. In the event that such health authority or Regulatory Agency contacts ZGEN with respect to such matters, ZGEN shall promptly inform NN. ZGEN shall in all cases provide copies to NN of all correspondence with such health authority or Regulatory Agency.

Section 13.20. Obligations of Novo.

(a) NN hereby appoints Novo to perform NN's research and development obligations under this Agreement, and Novo hereby accepts such appointment. Accordingly, NN and Novo shall be jointly and severally liable to ZGEN in the event of a failure of performance of NN's research and development obligations under this Agreement.

(b) Novo absolutely, irrevocably and unconditionally guarantees all payments that NN is required to make to ZGEN under this Agreement and guarantees the payment to ZGEN of any and all

damages, claims and losses incurred by ZGEN, as determined by a court from which no appeal has been or can be taken in an action against NN or Novo, arising out or related to the failure of NN to perform any of its obligations. The obligations of Novo under this **Section 13.20(b)** shall not be released, discharged or otherwise affected by (i) any assignment of or sublicense under this Agreement or any rights, interests, benefits or obligations thereunder by NN, whether by operation of law or otherwise and whether or not consented to by Novo or ZGEN or (ii) the amendment, modification or waiver of any of the terms or conditions of this Agreement. Novo expressly waives any and all rights, benefits or defenses under (A) any defense other than payment and satisfaction in full of all of the obligations of NN and (B) any claim or circumstance that constitutes a legal or equitable discharge of a guarantor or surety.

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IN WITNESS WHEREOF, the Parties hereto and Novo have each caused a duly authorized officer to sign this Agreement as of the Effective Date.

Novo Nordisk Health Care AG

By: _____ /Boov

Title: Chairman of the Board of Directors

By: _____ /Boov

Title: Vice President

ZymoGenetics, Inc.

By: _____

President and CEO

Novo Nordisk A/S

By: _____ /Boov

Title: Executive Vice President

By: _____ /Boov

Title: Executive Vice President