

# PATENT ASSIGNMENT

Electronic Version v1.1

Stylesheet Version v1.1

SUBMISSION TYPE:	NEW ASSIGNMENT				
NATURE OF CONVEYANCE:	Confirmatory License Agreement				
CONVEYING PARTY DATA					
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 80%; text-align: center; padding: 5px;">Name</td> <td style="width: 20%; text-align: center; padding: 5px;">Execution Date</td> </tr> <tr> <td style="padding: 5px;">AFFYMAX, INC.</td> <td style="padding: 5px;">06/27/2006</td> </tr> </table>	Name	Execution Date	AFFYMAX, INC.	06/27/2006	
Name	Execution Date				
AFFYMAX, INC.	06/27/2006				
RECEIVING PARTY DATA					
Name:	Takeda Pharmaceutical Company Limited.				
Street Address:	1-1 Doshomachi 4-chome Chuo-ku				
City:	Osaka				
State/Country:	JAPAN				
Postal Code:	540-8645				
PROPERTY NUMBERS Total: 26					
Property Type	Number				
Application Number:	60470246				
Application Number:	60470245				
Application Number:	60469996				
Application Number:	60469993				
Application Number:	60470244				
Application Number:	60627433				
Application Number:	60627432				
Application Number:	60687655				
Application Number:	60831049				
Application Number:	10844933				
Application Number:	10555868				
Application Number:	10555860				
Application Number:	11261157				
Application Number:	11271526				
Application Number:	11497569				

OP \$1040.00 60470246

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**PATENT**  
**REEL: 018375 FRAME: 0487**

Application Number:	11271524
Application Number:	11497547
Application Number:	11446593
PCT Number:	US0414888
PCT Number:	US0414887
PCT Number:	US0414886
PCT Number:	US0414889
PCT Number:	US0541113
PCT Number:	US0541112
PCT Number:	US0621845
Patent Number:	7084245

#### CORRESPONDENCE DATA

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ATTORNEY DOCKET NUMBER:	04279/8202152-000
NAME OF SUBMITTER:	Jessica Rojas

#### Total Attachments: 106

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[ \* ] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED

## COLLABORATION AND LICENSE AGREEMENT

This **COLLABORATION AND LICENSE AGREEMENT** (the “**Agreement**”) is entered into on June 27, 2006 (the “**Effective Date**”) between **AFFYMAX, INC.**, a Delaware corporation, with its principal place of business at 4001 Miranda Avenue, Palo Alto, CA 94304, U.S.A. (“**Affymax**”), and **TAKEDA PHARMACEUTICAL COMPANY LIMITED**, a company incorporated under the laws of Japan, with a place of business at 1-1, Doshomachi 4-chome, Chuo-ku, Osaka, 540-8645, Japan (“**Takeda**”). Affymax and Takeda are sometimes referred to herein individually as a “**Party**” and collectively as the “**Parties**”.

### RECITALS

**WHEREAS**, Affymax is a pharmaceutical company focused on the development of novel, synthetic peptide-based pharmaceutical products against targets for various diseases and conditions;

**WHEREAS**, Takeda is a worldwide pharmaceutical company engaged in the development, manufacturing and marketing of pharmaceutical products;

**WHEREAS**, Affymax has been developing the Product (as hereinafter defined), which contains a proprietary pegylated [ \* ] drug candidate known as Hematide™, for the treatment of anemia in patients with chronic kidney disease and cancer;

**WHEREAS**, Affymax and Takeda have entered into a collaboration for the development and commercialization of the Product in Japan for the treatment of anemia under the terms of the Japan Agreement (as hereinafter defined);

**WHEREAS**, Affymax and Takeda desire to establish a broad collaboration under this Agreement for the joint development and commercialization of the Product in the United States for the treatment of anemia in patients with chronic kidney disease and cancer and other indications as the Parties may jointly or unilaterally develop in such territory with Affymax serving as the primary responsible Party for the treatment of anemia in patients with chronic kidney disease and Takeda serving as the primary responsible Party for the treatment of anemia in patients with cancer, and to provide for the sole development by Takeda in other countries throughout the world, except for Japan (as contemplated under the Japan Agreement);

**WHEREAS**, the Parties desire that Affymax manufacture or have manufactured clinical and commercial supplies of the Bulk API (as hereinafter defined) and/or the Product and Takeda perform the Finished Manufacture (as hereinafter defined) for use by both Parties hereunder;

**WHEREAS**, Affymax and Takeda desire to co-commercialize the Product in the United States and share equally in the costs and efforts for the purpose of and in the profits resulting

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from marketing and sales of the Product in the United States and to provide for the payment by Takeda to Affymax of certain royalty payments on sales of the Product in the other territories of the world, except for Japan, in each case in accordance with the terms set forth below;

**WHEREAS**, Affymax desires to grant to Takeda exclusive rights to the Products and certain backup compounds in the United States and other countries of the world, except for Japan (which rights have separately been granted to Takeda), under this Agreement, and Takeda desires to obtain such rights in each case on the terms set forth below;

**NOW THEREFORE**, in consideration of the foregoing premises and mutual promises, covenants and conditions contained in this Agreement, the Parties agree as follows:

## **ARTICLE 1**

### **DEFINITIONS**

The terms in this Agreement with initial letters capitalized, whether used in the singular or the plural, shall have the meaning set forth below or, if not listed below, the meaning designated in places throughout this Agreement.

**1.1 “Additional Indication”** means any use for the Product in the Field, other than the Initial Indications.

**1.2 “Affiliate”** means, with respect to a particular Party, a person, corporation, partnership, or other entity that controls, is controlled by or is under common control with such Party. For the purposes of this definition, the word “control” (including, with correlative meaning, the terms “controlled by” or “under the common control with”) means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of fifty percent (50%) or more of the voting stock of such entity, or by contract or otherwise. Notwithstanding the foregoing, TAP Pharmaceutical Products Inc. shall not be deemed to be an Affiliate of Takeda.

**1.3 “Affymax House Marks”** means the Affymax names and logo as set forth in Exhibit A.

**1.4 “Affymax Know-How”** means all Information that is Controlled by Affymax or its Affiliates during the Term and is necessary or useful for the Development, manufacture or Commercialization of the Product. For clarity, Affymax Know-How excludes the Affymax Patents.

**1.5 “Affymax Patent”** means any Patent, including Affymax’s interest in any Joint Patent, that (a) is Controlled by Affymax or its Affiliates at any time during the Term, and (b) claims the Peptide, [ \* ], Hematide, Product or their manufacture or use, or any other invention that is otherwise necessary or useful for the Development, Finished Manufacture or Commercialization of the Product. The list of Affymax Patents as of the Effective Date is attached hereto as Exhibit B, and shall be from time to time amended and updated during the Term to incorporate the then-current Affymax Patents.

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**1.6 “Affymax Technology”** means the Affymax Patents and Affymax Know-How.

**1.7 “Alliance Representative”** has the meaning set forth in Section 2.7.

**1.8 “Anemia of Cancer”** means anemia in patients with cancer (but excluding Chemotherapy-Induced Anemia).

**1.9 “Backup Compound”** means any synthetic peptide-based [ \* ] ESA Controlled by Affymax as of the Effective Date and for [ \* ] years after the Effective Date, which such ESA: (i) has [ \* ], which are [ \* ] Hematide; and/or (ii) has a reasonable [ \* ] sufficient for the primary use of such product for the prevention, treatment or amelioration of anemia in humans. For the avoidance of doubt, Backup Compounds shall exclude any [ \* ] Product subject to Section 6.6(b). The initial list of the Backup Compounds is attached hereto as Schedule 1.9 and shall be updated from time to time by Affymax and provided to Takeda promptly. The list of the Backup Compounds thus updated shall include any synthetic peptide-based [ \* ] ESA which falls in the above definition which are discovered or developed by Affymax during the course of the Backup Research Agreement and thereafter.

**1.10 “Backup Research Agreement”** has the meaning set forth in Section 3.7.

**1.11 “Bulk API”** means Hematide in bulk form.

**1.12 “Business Day”** means any day other than (i) Saturday or Sunday or (ii) any other day on which banks in San Francisco, California, United States or Osaka, Japan are permitted or required to be closed.

**1.13 “Chemotherapy-Induced Anemia”** means anemia caused by chemotherapy treatments for cancer.

**1.14 “Claims”** has the meaning set forth in Section 11.1.

**1.15 “CTA”** means an application for Clinical Trial Authorization filed with a Regulatory Authority in the Licensed Territory to undertake clinical trials of an investigational new drug, the filing of which is necessary to commence or conduct clinical testing of a pharmaceutical product in humans in the Royalty Territory.

**1.16 “Commercial Expenses”** means those expenses incurred for the purpose of the Commercialization of the Finished Product in the U.S. which are consistent with the budget set forth in the U.S. Commercialization Plan and are specifically attributable to the Commercialization of Finished Products in the U.S., and shall consist of (i) Cost of Goods Sold, (ii) Pre-Marketing Expenses, (iii) Marketing Expenses, (iv) Distribution Expenses, (v) Clinical Phase IV and Related Expenses, (vi) Regulatory Expenses, (vii) the Launch Expense Allowance, (viii) Medical Science Liaison Expenses, and (ix) amounts paid to Third Party licensors as described in Section 8.6 (as such terms are defined in Exhibit J). Commercial Expenses shall exclude Development Expenses, even if incurred after the first commercial launch of a Finished Product in the U.S., and shall exclude any costs that are deductible from Net Sales under the

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definition thereof (e.g., distributor fees). For avoidance of doubt, any cost deducted in the calculation of Net Sales shall not be deducted in the calculation of the Commercial Expenses.

**1.17 “Commercialization”**, with a correlative meaning for **“Commercialize”**, means all activities undertaken before and after obtaining Regulatory Approval relating specifically to the pre-marketing, launch, promotion, marketing, sale, and distribution of a pharmaceutical product, including: (a) strategic marketing, sales force detailing, advertising, medical education and liaison, and market and product support; and (b) any Phase IV Clinical Trials, and (c) all customer support and Product distribution, invoicing and sales activities.

**1.18 “Confidential Information”** means, with respect to a Party, all confidential Information of such Party that is disclosed to the other Party under this Agreement, which may include specifications, know-how, trade secrets, legal information, technical information, drawings, models, business information, inventions, discoveries, methods, procedures, formulae, protocols, techniques, data, and unpublished patent applications, whether disclosed in oral, written, graphic, or electronic form. All Confidential Information disclosed by either Party pursuant to the Mutual Confidential Disclosure Agreement between the Parties dated September 30, 2005 shall be deemed to be such Party’s Confidential Information disclosed hereunder.

**1.19 “Control”** means, with respect to any material, Information, or intellectual property right, that a Party owns or has a license to such material, Information, or intellectual property right and has the ability to grant to the other Party access, a license, or a sublicense (as applicable) to such material, Information, or intellectual property right on the terms and conditions set forth herein without violating the terms of any agreement or other arrangement with any Third Party existing at the time such Party would be first required hereunder to grant to the other Party such access, license, or sublicense.

**1.20 “Cross-License Agreement”** means that certain Cross-License and License Option Agreement entered into by and among Nektar, Enzon, and Inhale Therapeutic Systems, Inc. on January 7, 2002, under which Nektar obtained certain rights under the Enzon Patents and which are sublicensed to Affymax by Nektar under the Nektar Agreement.

**1.21 “Detail” or “Detailing”** means, with respect to the Product, the communication by a Sales Representative during a Sales Call (a) involving face-to-face contact, (b) describing in a fair and balanced manner the Regulatory Authority-approved indicated uses and other relevant characteristics of the Product, (c) using the Promotional Materials in an effort to increase the prescribing and/or hospital ordering preferences of the Product for its approved indicated uses, and (d) made at such medical professional’s office, in a hospital, at marketing meetings sponsored by a Party for the Product or other appropriate venues conducive to pharmaceutical product informational communication where the principal objective is to place an emphasis, either primary or secondary, on the Product with such medical professional.

**1.22 “Develop” or “Development”** means all activities relating to preparing and conducting preclinical testing, toxicology testing, human clinical studies, regulatory affairs for obtaining the Regulatory Approvals, formulation development, process development for manufacture and associated validation, quality assurance and quality control activities (including qualification lots). Development shall exclude all Phase IV Clinical Trials.

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**1.23 “Development Budget”** means the budget of U.S. Development Expenses set forth in the U.S. Development Plan to be incurred by the Parties in connection with the performance of the U.S. Development Plan.

**1.24 “Development Expenses”** means (i) the U.S. Development Expenses, (ii) Manufacturing Development Expenses incurred by either Party for relevant activities performed on or after January 1, 2007, (iii) the Third Party milestone payments identified on Exhibit N (but not other milestones payable to Third Parties on account of the Development of the Product), (iv) the costs for Phase II Clinical Trial for Oncology Indications incurred by Takeda for relevant activities conducted on or after the Effective Date until the end of December 31, 2006, (v) the price from Affymax to Takeda of Bulk API and/or the Finished Product used for the U.S. Development of the Product as well as the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Bulk API, and (vi) the cost incurred by Takeda for the Finished Manufacture of the Product used for the U.S. Development of the Product as well as the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Product; but excluding, [ \* ]. For clarity, any amounts payable by Affymax for ongoing clinical, non-clinical, preclinical and other trials regarding the Product performed on or before December 31, 2006 shall not be included as Development Expenses and shall be borne by Affymax.

**1.25 “Dialysis CKD Anemia”** means use of the Product in the prevention, treatment or amelioration of anemia in patients with chronic kidney disease who are on dialysis.

**1.26 “Diligent Efforts”** means, with respect to a Party’s obligation under this Agreement to Develop or Commercialize a Product, the level of efforts required to carry out such obligation in a sustained manner consistent with the efforts a similarly situated biopharmaceutical company (in the case of Affymax) or multinational pharmaceutical company (in the case of Takeda) devotes to a product of similar market potential, profit potential or strategic value within its portfolio, based on conditions then prevailing. Without limiting the foregoing, Diligent Efforts requires, with respect to such an obligation, that the Party: (a) within a reasonable time assign responsibility for such obligation to specific employee(s) who are held accountable for progress and monitor such progress on an on-going basis, (b) set and consistently seek to achieve specific, meaningful and measurable objectives for carrying out such obligation, and (c) consistently make and implement decisions and allocate resources designed to advance progress with respect to such objectives.

**1.27 “[ \* ]”** means Affymax’s proprietary ESA peptide [ \* ] [ \* ] with the chemical structure attached hereto as Exhibit C.

**1.28 “Dollar”** means a U.S. dollar, and “\$” shall be interpreted accordingly.

**1.29 “EMEA”** means the European Agency for the Evaluation of Medicinal Products, or any successor thereto, which is responsible for coordinating the centralized system for Regulatory Approval of pharmaceutical products in the European Union and the European Economic Area and recommending to the European Commission (the “EC”) that the EC grant

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Regulatory Approval of certain pharmaceutical products in the EU and EEA under such centralized system.

**1.30 “Enzon”** means Enzon Pharmaceuticals, Inc., a Delaware corporation having its principal offices at 685 Route 202/206, Bridgewater, New Jersey 08807, USA.

**1.31 “Enzon Patents”** means the Patents licensed from Enzon and identified on Exhibit B.

**1.32 “ESA”** means erythropoiesis stimulating agent.

**1.33 “European Union” or “EU”** means all of the European Union member states as of the applicable time during the Term.

**1.34 “Existing Third Party License Agreements”** has the meaning set forth in Section 6.7.

**1.35 “FDA”** means the U.S. Food and Drug Administration or its successor.

**1.36 “FD&C Act”** means the U.S. Federal Food, Drug and Cosmetic Act, as amended.

**1.37 “Field”** means the prevention, treatment or amelioration of any disease or condition in humans.

**1.38 “Finance Subcommittee”** has the meaning set forth in Section 2.6(c).

**1.39 “Finished Manufacture”** means the manufacture (and all reasonably necessary testing, including release and, as appropriate, stability testing) of Finished Product from Bulk API.

**1.40 “Finished Product”** means a Product that has been filled into vials, syringes or manufactured into other pharmaceutical presentations for administration, finished and labeled for use in clinical trials or for commercial purposes in accordance with the applicable specifications and legal requirements.

**1.41 “First Commercial Sale”** means, with respect to a particular country and the Product, the first sale to a Third Party of the Product in such country after Regulatory Approval has been obtained in such country.

**1.42 “Fiscal Year”** means the twelve (12)-month period commencing on April 1 of a given year and ending on March 31 of the following year.

**1.43 “Good Clinical Practices” or “GCP”** means the then-current good clinical practice standards, practices and procedures promulgated or endorsed by the FDA as set forth in the guidelines entitled “Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance,” including related regulatory requirements imposed by the FDA, and comparable regulatory standards, practices and procedures in jurisdictions outside the U.S., in each case as they may be updated from time to time.

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**1.44 “Good Laboratory Practices” or “GLP”** means the then-current good laboratory practice standards promulgated or endorsed by the FDA as defined in 21 C.F.R. Part 58, and comparable regulatory standards in jurisdictions outside the U.S., in each case as they may be updated from time to time.

**1.45 “Good Manufacturing Practices” or “GMP”** means the then-current good manufacturing practices required by the FDA, as set forth in the FD&C Act and the regulations promulgated thereunder, for the manufacture and testing of pharmaceutical materials, and comparable Laws applicable to the manufacture and testing of pharmaceutical materials in jurisdictions outside the U.S., including without limitation the guideline promulgated by the International Conference on Harmonization designated ICH Q7A, entitled “Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients” and the regulations promulgated thereunder, in each case as they may be updated from time to time.

**1.46 “Governmental Authority”** means any multi-national, federal, state, local, municipal or other government authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, court or other tribunal).

**1.47 “Hematide”** means Affymax’s proprietary pegylated ESA drug candidate referred to internally as [ \* ], consisting of the [ \* ] attached to the Reagent.

**1.48 “IND”** means (a) an Investigational New Drug application as defined in the FD&C Act and applicable regulations promulgated thereunder by the FDA.

**1.49 “Information”** means any data, results, technology, business information, and information of any type whatsoever, in any tangible or intangible form, including, without limitation, know-how, trade secrets, practices, techniques, methods, processes, inventions, developments, specifications, formulations, formulae, materials or compositions of matter of any type or kind (patentable or otherwise), software, algorithms, marketing reports, expertise, technology, test data (including pharmacological, biological, chemical, biochemical, toxicological, preclinical and clinical test data), analytical and quality control data, stability data, other study data and procedures.

**1.50 “Initial Indications”** means the Oncology Indications and the Renal Indications.

**1.51 “[ \* ]”** means any [ \* ] agent, [ \* ], [ \* ], developed under an Affymax research or development program that is used to [ \* ], either directly or indirectly, from [ \* ] due to [ \* ], or any other such [ \* ], including [ \* ]; or to treat an [ \* ], directly or indirectly, to such [ \* ] with the intent of [ \* ], subject to Section 6.6(b). For clarity, an [ \* ] may act as an agonist or antagonist through the EPO receptor or related receptors, or through other known or unknown receptors on the surface of the cells in question, or it may act independently of a cell surface receptor.

**1.52 “Internal Expenses”** means any costs for employees (to be charged at a fixed rate to be agreed by the Parties from time to time), overhead, or other internal handling incurred by a Party, which expenses are generally consistent with the U.S. Development Plan and are specifically attributable to the U.S. Development.

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**1.53 “Japan Agreement”** means the Collaboration and License Agreement dated as of February 13, 2006 between Affymax and Takeda under which the parties have entered into a collaboration for the development and commercialization of the Product in Japan for the treatment of anemia.

**1.54 “Joint Steering Committee” or “JSC”** means the committee formed by the Parties as described in Section 2.3(a).

**1.55 “Joint Inventions”** has the meaning set forth in Section 9.1.

**1.56 “Joint Patent”** has the meaning set forth in Section 9.3(c).

**1.57 “Laws”** means all relevant laws, statutes, rules, regulations, guidelines, ordinances and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, domestic or foreign.

**1.58 “Level 1 Market”** means any of the following countries: [ \* ].

**1.59 “Level 2 Market”** means any of the following countries: [ \* ].

**1.60 “Licensed Territory”** means worldwide except Japan, its territories and possessions, as adjusted from time to time pursuant to Section 3.5.

**1.61 “Major EU Market Country”** means any of the following countries: [ \* ].

**1.62 “Manufacturing Costs”** has the meaning set forth in Exhibit J.

**1.63 “Manufacturing Development”** means any of the following with respect to Bulk API or Finished Product: manufacturing process development and validation, process improvements, associated analytical development and validation and the manufacture and testing of clinical and stability or consistency lots (including process development, qualification, QA, and test batches).

**1.64 “Manufacturing Development Expenses”** means any costs incurred by a Party to a Third Party after the Effective Date for the Manufacturing Development.

**1.65 “Marketing Authorization Application” or “MAA”** means an application for Regulatory Approval (but excluding Pricing Approval) in any particular jurisdiction other than the U.S.

**1.66 “NDA”** means a New Drug Application filed with the FDA for Regulatory Approval of a product in the U.S.

**1.67 “Nektar”** means Nektar Therapeutics AL Corporation, an Alabama corporation having its principal place of business at 490 Discovery Drive, Huntsville, AL 35806, USA.

**1.68 “Nektar Agreement”** means that certain License, Manufacturing, and Supply Agreement between Affymax and Nektar Therapeutics AL, dated as of April 8, 2004, under

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which Affymax is granted a right, license and/or sublicense under certain of Nektar's patents and technologies and Enzon Patents, which patents are included in the Affymax Patents.

**1.69 "Net Sales"** means, with respect to a particular time period, the total amounts received or invoiced by Takeda, its Affiliates and their respective sublicensees for sales of Finished Product made during such time period to unaffiliated Third Parties, less the following deductions to the extent actually allowed or incurred with respect to such sales:

(a) discounts, including cash and quantity discounts, charge-back payments, and rebates actually granted or administrative fees actually paid to trade customers, patients (including those in the form of a coupon or voucher), managed health care organizations, pharmaceutical benefit managers, group purchasing organizations, federal, state, or local government and the agencies, purchasers and reimbursers of managed health organizations, pharmaceutical benefit managers, group purchasing organizations, or federal, state or local government; provided, however, that: (i) the aggregate of such discounts, charge-back payments and rebates in each country of the Royalty Territory shall not exceed [ \* ] of the amounts received or invoiced in such country; and, (ii) if such limit of [ \* ] in a country of the Royalty Territory is not sufficient or appropriate due to significant amount or percentage of discounts, charge-back payments or rebates mandatorily required by Governmental Authorities in such country, and/or, if such limit is not sufficient for adequately maintaining the competitive position of the Products in such country, then the Parties shall confer in good faith regarding whether any increase in such limit is appropriate under the circumstances;

(b) credits or allowances actually granted upon prompt payment or claims, bad debts and losses actually incurred as a result of actual write-offs of uncollectible customer accounts, damaged goods, rejections or returns of such Product, including in connection with recalls;

(c) packaging, freight, postage, shipping, transportation, warehousing, handling and insurance charges, credit card processing fees and any customary payments with respect to the Products actually made to wholesalers or other distributors, in each case actually allowed or paid for distribution and delivery of Product, to the extent billed or recognized; and

(d) taxes (other than income taxes), duties, tariffs or other governmental charges levied on the sale of such Product, including, without limitation, value-added and sales taxes.

Notwithstanding the foregoing, amounts received or invoiced by Takeda, its Affiliates, or their sublicensees for the sale of Finished Product among Takeda, its Affiliates or their respective sublicensees for resale shall not be included in the computation of Net Sales hereunder. In any event, any amounts received or invoiced by Takeda, its Affiliates, or their sublicensees shall be accounted for only once. Net Sales shall be accounted for in accordance with standard Takeda practices for operation by Takeda, its Affiliates or sublicensees, as practiced in the relevant country in the Licensed Territory, but in any event in accordance with generally accepted accounting principles, consistently applied in such country in the Licensed Territory. Net Sales shall exclude any samples of Product transferred or disposed of at no cost for promotional or

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educational purposes, and the cost for such samples transferred or disposed of in the U.S. shall be deemed to be included in the Commercial Expenses.

Further, the Parties agree to negotiate in good faith for an equitable determination of the Net Sales of the Product in the event Takeda, its Affiliates or their sublicensees sells the Product in such a manner that gross sales of the Product are not readily identifiable (*e.g.*, for Product to be sold as a combination product or bundling with other products).

**1.70 “Oncology Indications”** means, collectively, Anemia of Cancer and Chemotherapy-Induced Anemia.

**1.71 “Patents”** means (a) pending patent applications, including provisional patents, issued patents, utility models and designs; and (b) extensions, reissues, substitutions, confirmations, registrations, validations, re-examinations, additions, continuations, continued prosecution applications, requests for continued examination, continuations-in-part, or divisions of or to any patents, patent applications, utility models or designs.

**1.72 “Patent Term Extension”** means any term extensions, supplementary protection certificates and equivalents thereof offering patent protection beyond the initial term with respect to any issued patents.

**1.73 “PDE”** shall mean one Primary Position Detail (as defined below), two Secondary Position Details (as defined below) or five Tertiary Position Details (as defined below).

**1.74 “PEG”** means poly(ethylene) glycol or a derivative thereof.

**1.75 “Peptide”** means that certain peptide ESA known as [ \* ], the chemical structure of which is attached hereto as Exhibit D.

**1.76 “Phase I Clinical Trial”** means a small scale trial of a pharmaceutical product on subjects that generally provides for the first introduction into humans of such product with the primary purpose of determining safety, metabolism and pharmacokinetic properties and clinical pharmacology of such product.

**1.77 “Phase II Clinical Trial”** means a small scale clinical trial of a pharmaceutical product on patients, including possibly pharmacokinetic studies, the principal purposes of which are to make a preliminary determination that such product is safe for its intended use and to obtain sufficient information about such product’s efficacy to permit the design of further clinical trials.

**1.78 “Phase III Clinical Trial”** means one or more clinical trials on sufficient numbers of patients, which trial(s) are designed to (a) establish that a drug is safe and efficacious for its intended use; (b) define warnings, precautions and adverse reactions that are associated with the drug in the dosage range to be prescribed; and (c) support Regulatory Approval of such drug.

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**1.79 “Phase IV Clinical Trial”** means a clinical trial of a Product, possibly including pharmacokinetic studies, which trial is (a) not required in order to obtain Regulatory Approval of the Initial Indication or the Joint Additional Indication; (b) required by the Regulatory Authority as mandatory to be conducted on or after the Regulatory Approval of the Initial Indications or the Joint Additional Indication, and (c) conducted voluntarily by a Party to enhance marketing or scientific knowledge of the Product (*e.g.*, providing additional drug profile, safety data or marketing support information, or supporting expansion of Product Labeling or conducted due to a request or requirement of a Regulatory Authority).

**1.80 “Pre-Dialysis CKD Anemia”** means use of the Product in the prevention, treatment or amelioration of anemia in patients with chronic kidney disease who are not on dialysis.

**1.81 “Pricing Approval”** means such approval, agreement, determination or governmental decision establishing prices for the Product that can be charged to consumers and shall be reimbursed by Governmental Authorities in regulatory jurisdictions where the Governmental Authorities or Regulatory Authorities approve or determine pricing of pharmaceutical products for reimbursement or otherwise.

**1.82 “Primary Position Detail”** means a Detail during which (i) the applicable Product is discussed either itself or along with other pharmaceutical products, (ii) key product attributes of such Product are verbally promoted in the first position on such Detail, and (iii) such Product is given the majority of the emphasis during the presentation. For clarity, no more than one Detail during a Sales Call shall be considered a Primary Position Detail.

**1.83 “Product”** means a pharmaceutical preparation in any formulation that contains Hematide or, subject to the terms of Section 3.11, a Replacement Product Candidate as an active ingredient. In addition, an Additional Product shall become a Product pursuant to the terms of Section 3.12.

**1.84 “Product Complaint”** means any written, verbal or electronic expression of dissatisfaction regarding the Product, including without limitation reports of actual or suspected product tampering, contamination, mislabeling or inclusion of improper ingredients.

**1.85 “Product Infringement”** has the meaning set forth in Section 9.5(b).

**1.86 “Product Labeling”** means (a) the full prescribing information for the Product approved by the applicable Regulatory Authority, and (b) all labels and other written, printed or graphic information included in or placed upon any container, wrapper or package insert used with or for the Product.

**1.87 “Product Subcommittee”** has the meaning set forth in Section 2.6(b).

**1.88 “Product Trademark”** means the mark “HEMATIDE” and any logos or symbols incorporating such mark and any product trademark selected pursuant to Section 5.11.

**1.89 “Profit Equalization Payment”** means the amount payable by one Party to the other to effect an allocation of the U.S. Product Profit between the Parties as described in Section 8.4 and the final financial statement approved by the JSC for a calendar quarter. By way of example, assuming an equal allocation of profits and losses, if Takeda has an operating profit of 40 and Affymax has an operating loss of 10, then the Profit Equalization Payment made by Takeda to Affymax shall be 25.

**1.90 “Promotional Materials”** means all Sales Representative training materials and all written, printed, graphic, electronic, audio or video presentations of information, including, without limitation, journal advertisements, sales visual aids, formulary binders, reprints, direct mail, direct-to-consumer advertising, internet postings, broadcast advertisements and sales reminder aides (for example, note pads, pens and other such items) intended for use or used by or on behalf of Takeda or its Affiliates, sublicensees or licensees in connection with any promotion of a Product in the Licensed Territory (all to the extent applicable for the Commercialization in the Licensed Territory), but excluding Product Labeling.

**1.91 “Reagent”** means the reagent described in Exhibit E.

**1.92 “Regulatory Approvals”** means all approvals (including without limitation supplements, amendments, and Pricing Approvals), licenses, registrations or authorizations of any national, supra-national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, necessary for the manufacture, distribution, use or sale of a pharmaceutical product in a given regulatory jurisdiction.

**1.93 “Regulatory Authority”** means, in a particular country or jurisdiction, any applicable Governmental Authority involved in granting Regulatory Approval in such country or jurisdiction, including without limitation, in the U.S., the FDA and any other applicable Governmental Authority in the U.S. having jurisdiction over the Product, and, in the European Union, the EMEA and any other applicable Governmental Authority having jurisdiction over the Product.

**1.94 “Regulatory Materials”** means regulatory applications, submissions, notifications, registrations, Regulatory Approvals or other submissions made to or with a Regulatory Authority that are necessary or reasonably desirable in order to develop, manufacture, market, sell or otherwise commercialize the Product in a particular country, territory or possession. Regulatory Materials include, without limitation, INDs, CTAs and MAAs, NDAs, and amendments and supplements for any of the foregoing, and applications for Pricing Approvals.

**1.95 “Renal Indications”** means, collectively, Pre-dialysis CKD Anemia and Dialysis CKD Anemia.

**1.96 “Replacement Product Candidate”** means any Backup Compound linked to PEG [ \* ] (including [ \* ]).

**1.97 “Royalty Territory”** means all countries in the Licensed Territory other than the U.S.

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**1.98 “ROW Commercialization Plan”** has the meaning set forth in Section 5.2(b).

**1.99 “ROW Development”** means the Development of the Products specifically required only in a certain country or countries of the Royalty Territory to support Regulatory Approval of the Product for the Initial Indications and/or the Joint Additional Indications, if any, in such country or countries of the Royalty Territory, irrespective of the country wherein a study thereof is conducted. For the purpose of this definition, Manufacturing Development shall be excluded from the ROW Development.

**1.100 “Sales Call”** means a personal visit by a Sales Representative to one or several medical professional(s) having prescribing authority in the part of the Field for the indications in which the Product is approved, as well as to other individuals or entities that have significant impact or influence on prescribing decisions in the part of the Field in which the Product is approved during which such Sales Representative Details the Product.

**1.101 “Sales Representative”** means a pharmaceutical sales representative engaged or employed by either Party to conduct Detailing and other promotional efforts with respect to the Product, including contract sales organizations of such Party.

**1.102 “Secondary Position Detail”** shall mean a Detail during which key product attributes of a Product are verbally promoted and detailed in the second position on such Detail; provided, however, that no more than one presentation in any Detail shall be considered a Secondary Position Detail, which shall be the presentation on which the second-most time is spent during the Detail.

**1.103 “Sole Inventions”** has the meaning set forth in Section 9.1.

**1.104 “Supply Agreement”** has the meaning set forth in Section 7.3.

**1.105 “Takeda Know-How”** means all Information that is Controlled by Takeda or its Affiliates during the Term under this Agreement and is necessary or useful for the Development, manufacture or Commercialization of the Product. For clarity, Takeda Know-How excludes Takeda Patents.

**1.106 “Takeda Patent”** means any Patent, including Takeda’s interest in any Joint Patent, that (a) is Controlled by Takeda or its Affiliates at any time during the Term under this Agreement, and (b) claims the Peptide, [ \* ], Bulk API and/or Product or any method or composition, or the manufacture or use of the Peptide, [ \* ], Bulk API and/or Product.

**1.107 “Takeda Technology”** means the Takeda Patents and Takeda Know-How.

**1.108 “Tertiary Position Detail”** shall mean a Detail during which key product attributes of a Product are verbally promoted and detailed in the third or lesser position on such Detail.

**1.109 “Term”** means the term of this Agreement, as determined in accordance with Article 13.

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**1.110 "Third Party"** means any entity other than Affymax or Takeda or an Affiliate of either of them.

**1.111 "U.S."** means the United States of America and its possessions and territories.

**1.112 "U.S. Development"** means the Development of the Products conducted hereunder for the primary purpose of supporting (whether pivotal or not) the U.S. Regulatory Approvals for the Initial Indications and/or the Joint Additional Indications, if any, irrespective of the country wherein a study thereof is conducted and irrespective whether the result of which is also used for the purpose of supporting the Regulatory Approvals in the Royalty Territory. For the purpose of this definition, Manufacturing Development shall be excluded from the U.S. Development.

**1.113 "U.S. Commercialization Plan"** has the meaning set forth in Section 5.2(a).

**1.114 "U.S. Development Expenses"** means any amounts payable by a Party for obligations to a Third Party for the U.S. Development performed on or after January 1, 2007, which expenses are generally consistent with the Development Budget.

**1.115 "U.S. Development Plan"** means the plan of the U.S. Development. The initial U.S. Development Plan is attached hereto as Exhibit H. Exhibit H may be from time to time added or modified by the JSC.

**1.116 "U.S. Product Profit"** means the profits or losses resulting from the Commercialization of the Product in the U.S. and shall be equal to Net Sales of the Product in the U.S., less Commercial Expenses.

**1.117 "Valid Claim"** means (a) an unexpired claim of an issued patent that has not been disclaimed, revoked or held to be invalid or unenforceable by a court or other authority of competent jurisdiction, from which decision no appeal can be further taken; or (b) a claim of a pending patent application.

## **ARTICLE 2**

### **MANAGEMENT**

**2.1 Collaboration Overview.** The Parties desire and intend to collaborate with respect to the Development and Commercialization of the Product in the Licensed Territory, as and to the extent set forth in this Agreement. It is understood and acknowledged by each Party that such Party shall participate in the clinical development of the Product for identified indications, including the Initial Indications, in the Licensed Territory pursuant to an agreed-upon U.S. Development Plan. The Parties shall share the development costs incurred in connection with the performance of the U.S. Development Plan, as set forth in, and in accordance with, Article 3. Takeda shall bear the development costs incurred in connection with the performance of the ROW Development, as set forth in, and in accordance with, Article 3. Affymax shall be primarily responsible for obtaining and maintaining Regulatory Approval of the Product in the Field in the U.S. based on the then-current U.S. Development Plan, and

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Takeda shall be solely responsible for obtaining and be solely entitled to obtain and maintain Regulatory Approval of the Product in the Field in the Royalty Territory. In the U.S., the Parties shall co-promote the Product for the Initial Indications and share profits from the Initial Indications equally, with Affymax primarily participating in the sales and marketing efforts in the Renal Indications, subject to the payment obligations in Article 8 and the other terms of this Agreement. Takeda shall have the exclusive right to Commercialize the Product in the Royalty Territory, subject to the payment obligations in Article 8 and the other terms of this Agreement. Each Party understands and agrees that it is to the Parties' mutual benefit to maximize the commercial potential of the Product as far as commercially reasonably possible, and accordingly, that time is of the essence in addressing the market for the Product in the Field and the Licensed Territory.

**2.2 Commitment to U.S. Development Plan.** Each Party agrees and acknowledges that, by entering into this Agreement, it shall fund, as and to the extent set forth in Article 3, the Development of the Product in the Initial Indications pursuant to the U.S. Development Plan, and shall use Diligent Efforts to conduct the activities assigned to such Party in the U.S. Development Plan, with the JSC overseeing the implementation of such plan. Neither Party shall be obligated to expend any funds with respect to or participate in any clinical trials in support of any Additional Indications, except as provided in Section 3.10. The conduct of clinical trials and development activities in support of any such Additional Indications and Commercialization of the Product for such indications, if any, shall be governed by Section 3.10.

### **2.3 Joint Steering Committee.**

**(a) Formation and Role.** The Parties hereby establish a Joint Steering Committee that shall monitor and coordinate communication regarding the Parties' performance under this Agreement to Develop, obtain Regulatory Approval for and Commercialize the Product in the Field. The role of the JSC shall be:

**(i)** to review the overall strategy for Developing and seeking Regulatory Approval for, manufacturing, and Commercializing the Product in the Licensed Territory and in the Field;

**(ii)** to facilitate the exchange of information between the Parties with respect to the activities hereunder for the Licensed Territory and to establish procedures for the efficient sharing of information and materials necessary for each Party's Development and Commercialization of the Product hereunder, consistent with this Agreement;

**(iii)** to review, approve, and, if necessary, amend the U.S. Development Plan, the Development Budget and the U.S. Commercialization Plan (including related budget);

**(iv)** to review the plan and the summary budget for the ROW Development to the extent customarily generated by or available to Takeda from its Affiliates or sublicensees for its internal purposes with respect to the applicable countries in the Royalty Territory (all Level 1 Markets and Level 2 Markets wherein Takeda decides to Develop the Product, as described in further detail in Section 3.5) and the ROW Commercialization Plan and

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provide comments regarding the content and implementation of such plans, which comments shall not be controlling but shall be considered by Takeda in good faith;

(v) to monitor the Parties' performance against the then-current U.S. Development Plan and Commercialization Plans;

(vi) to create subcommittees as the JSC may find necessary or desirable from time to time for implementation of the Development and Commercialization hereunder;

(vii) to oversee the activities of subcommittees created under this Agreement, and to seek to resolve any issues that such subcommittees cannot resolve;

(viii) without reducing Affymax's obligation to obtain and maintain the Affymax Patents and/or the Product Trademark provided for herein, to provide a forum to evaluate strategies for obtaining, maintaining and enforcing patent and trademark protection for the Product in the Licensed Territory; and

(ix) to perform such other functions as appropriate to further the purposes of this Agreement, as determined by the Parties.

**(b) Guiding Principles.** The JSC shall perform its responsibilities under this Agreement based on the principles of prompt and diligent Development and Commercialization of the Product in the Licensed Territory, consistent with good pharmaceutical practices and the maximization, to a commercially reasonable extent, of long-term profits derived from the sale of the Product in the Licensed Territory. The JSC shall have only the powers assigned expressly to it in this Article 2 and elsewhere in this Agreement, and the JSC shall not have any power to amend, modify or waive compliance with this Agreement. For clarity, with regard to the Development and the Commercialization of the Product in the Royalty Territory, Takeda shall be entitled to develop and modify the plans and budgets therefor at its discretion, subject only to Takeda's obligations as provided in Section 3.5 and Article 4, and the JSC shall not be entitled to approve or disapprove such plans and budgets.

**2.4 JSC Membership.** Each Party shall have an equal number of representatives on the JSC, who initially shall be the eight (8) individuals at the [ \* ] (or other equivalent individuals having senior decision-making authority over JSC matters) as set forth in Exhibit F. The JSC may change its size from time to time by mutual consent of the Parties, provided that the JSC shall at all times consist of an equal number of representatives of each of Affymax and Takeda. Either Party may designate substitutes for its representatives if one (1) or more of such Party's designated representatives are unable to be present at a meeting. From time to time each Party may replace its representatives by written notice to the other Party specifying the prior representative(s) and their replacement(s). The initial representatives and any substitutes or replacements shall be designated consistent with the following principles: one (1) representative shall have appropriate expertise in the clinical Development of pharmaceutical products, one (1) representative shall have appropriate expertise in Commercialization of pharmaceutical products, and one (1) representative shall have expertise appropriate to the then-current state of Product Development or Commercialization; *provided that* the JSC may vary the expertise required for JSC representatives of each Party as it deems appropriate as the Parties gain experience with the

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Product, but in any event at least one (1) of such representatives on the JSC shall be at the [ \* ] in each of the Party's organizations. Affymax shall select one (1) of its representatives as the initial chairperson of the JSC. On April 1 of each year after the Effective Date, the Parties shall rotate designation of the chairperson for the commencing year. The chairperson shall be responsible for (i) calling meetings, and (ii) preparing and circulating an agenda for the upcoming meeting, but shall have no special authority over the other members of the JSC, and shall have no additional voting rights.

## **2.5 JSC Meetings, Decisions and Actions.**

(a) **Meetings.** The JSC shall hold at least three (3) meetings per year (at least two (2) of which shall be held in person) on such dates at such times each year as it elects. Meetings of the JSC shall be effective only if at least two (2) representatives of each Party are present or participating. Each Party shall bear the expense of its respective members' participation in JSC meetings. The Chairperson of the JSC shall be responsible for preparing and issuing minutes of each such meeting within thirty (30) days thereafter. Such minutes shall not be finalized until each Party reviews and confirms the accuracy of such minutes in writing; provided that any minutes shall be deemed approved unless a member of the JSC objects to the accuracy of such minutes within [ \* ] after the circulation of the minutes by the Chairperson. With the prior consent of both Parties' representatives (such consent not to be unreasonably withheld or delayed), other representatives of each Party or Third Parties involved with the Products may attend meetings as nonvoting participants.

(b) **Decision Making.** Except as expressly provided in this Section 2.5, actions to be taken by the JSC shall be taken only following unanimous vote, with each Party having one (1) vote.

(c) **Disputes.** If the members of the JSC cannot reach a unanimous decision with respect to matters delegated to it under this Article 2 (including without limitation any issue involving clinical trial design, priority of clinical trials, timelines, and the like, or the approval of any component of an amended or updated U.S. Development Plan or U.S. Commercialization Plan) for a period in excess of [ \* ] Business Days from the discussion at the JSC, unless the Parties agree to prolong such time period, the matter shall be referred to two appropriately qualified senior executive officers of the Parties, who shall attempt resolution by good faith negotiations for at least [ \* ] after such referral. If the senior executive officers designated by the Parties are not able to resolve such dispute within such [ \* ] period, then such dispute shall be finally decided by expedited arbitration in accordance with the terms described on Exhibit M, except that disputes described in Section 3.10(c) shall not be subject to such arbitration procedure.

## **2.6 Subcommittees.**

(a) The JSC may, from time to time, form any subcommittees as it may desire. Each such subcommittees shall have those responsibilities, and operate in accordance with the procedures, established by the JSC and shall report the results of its activities to the JSC. Each subcommittee shall provide the JSC with guidance and consultation regarding such

subcommittee's area of expertise; however, all final decision-making shall be the responsibility of the JSC, in accordance with the terms of Section 2.4.

(b) The Parties hereby establish a Product Subcommittee (**"Product Subcommittee"**) to oversee and manage the Development, Regulatory Approval, and Commercialization of the Product in accordance with the U.S. Development Plan, and to coordinate such U.S. Development with the Development activities of Takeda in the Royalty Territory. Each Party shall have an equal number of representatives on such subcommittee. The role of the Product Subcommittee shall be:

(i) to draft amendments or updates to the U.S. Development Plan and U.S. Commercialization Plan and present such amendments or updates to the JSC for review and approval;

(ii) to develop the overall strategy for Product Development and Commercialization activities in the U.S. performed hereunder;

(iii) to facilitate the flow of information between the Parties with respect to the Development, Regulatory Approval, and Commercialization of the Product hereunder; and

(iv) to perform such other functions as appropriate to further the purposes of this Agreement as determined by the JSC.

(c) The Parties hereby establish a Finance Subcommittee (**"Finance Subcommittee"**) to oversee the implementation and assist the JSC and other subcommittees with budgetary, financial and accounting issues arising out of the Development, Regulatory Approval, and Commercialization of the Product in accordance with the terms of this Agreement. Each Party shall have an equal number of representatives on such subcommittee. The role of the Finance Subcommittee shall be:

(i) to coordinate with the JSC and other subcommittees as applicable regarding the preparation and submission of budgets for the Development and Commercialization of the Product in the U.S.;

(ii) to develop specific schedules, procedures and methods to implement the financial reporting and reconciliation provisions of this Agreement; and

(iii) to perform such other functions as appropriate to further the purposes of this Agreement as determined by the JSC.

**2.7 Alliance Representative.** Each Party has designated on Exhibit F an appropriate employee to facilitate communication and coordination of the Parties' activities under this Agreement relating to the Product and to provide support and guidance to the JSC (each, an **"Alliance Representative"**). From time to time each Party may replace its Alliance Representative by prior written notice to the other Party specifying the replacement.

**2.8 Royalty Territory Information Sharing.** Without limiting any other provisions of this Agreement, the Parties acknowledge and agree that Takeda shall provide Affymax, through the JSC, with periodic updates regarding the Development and Commercialization activities undertaken by Takeda in or for the Royalty Territory (such updates to be provided quarterly if available or, otherwise, semi-annually) including summary plan of ROW Development and ROW Commercialization Plans for such activities (which such plans shall include summary financial information in each case to the extent customarily generated by or available to Takeda from its Affiliates or sublicensees for its internal purposes, with respect to such activities in the Royalty Territory, but subject to Takeda's right to redact or exclude detailed commercially-sensitive and proprietary information). In addition, Takeda shall provide such additional information regarding the ROW Development and Commercialization of the Product in the Royalty Territory as may be reasonably requested by Affymax and reasonably acceptable to Takeda from time to time.

### **ARTICLE 3**

#### **CLINICAL AND NON-CLINICAL PRODUCT DEVELOPMENT**

**3.1 Overview.** The Parties shall Develop the Product in the Initial Indications in the Licensed Territory as provided in this Article 3 and in accordance with the then-current U.S. Development Plan. The initial U.S. Development Plan sets forth the Development activities to be performed by each Party under this Agreement in connection with the submission for Regulatory Approval of the Product in the Initial Indications for the U.S. and attached hereto as Exhibit H (assuming that the results of such activities will at least be used in EU as well). The summary plan of the ROW Development and future updates thereof shall be submitted to the JSC for review (not for approval) in accordance with Section 2.8. Without limiting the generality of the foregoing, the Parties shall have the following Development obligations for the Product:

(a) Affymax shall be responsible for all ongoing clinical, non-clinical, preclinical and other trials regarding the Product that are listed on Exhibit G and shall provide Takeda the data obtained therein as provided in Section 4.1;

(b) Affymax shall be primarily responsible for implementing the clinical trials of the Product for Regulatory Approval in the Renal Indications pursuant to the U.S. Development Plan; and

(c) Takeda shall be (i) primarily responsible for implementing the clinical trials of the Product for Regulatory Approval in the Oncology Indications pursuant to the U.S. Development Plan, and (ii) solely responsible for the ROW Development of the Product for Regulatory Approval in all Initial Indications in the Royalty Territory (other than pursuant to the U.S. Development Plan) wherein Takeda Develops and Commercializes the Product.

**3.2 U.S. Development Plan.** The initial U.S. Development Plan for the Initial Indications has been agreed upon by the Parties and is attached hereto as Exhibit H and incorporated herein by reference. The U.S. Development Plan shall contain the following

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information for the Product for each Initial Indication in the Licensed Territory, to the extent such information is available:

(a) the proposed overall plan for Development for the Product for the Initial Indications (and each Joint Additional Indication pursued pursuant to Section 3.10) to support Regulatory Approval in the U.S. (assuming that the results of such activities will at least be used in EU as well);

(b) the Development Budget, which shall include a three (3)-year rolling budget of U.S. Development Expenses (including a detailed binding budget for the first year thereof and a non-binding forecast for subsequent two (2) years based on the then-current U.S. Development Plan);

(c) scope and target timelines for the Parties' performance of all studies within the U.S. Development, including without limitation, clinical trial protocols, additional preclinical tests (including any and all carcinogenicity and toxicology studies), Finished Product stability studies, enrollment numbers and submission dates;

(d) estimated dates of meetings with FDA for the Product; and

(e) the Parties' forecasts of their respective needs for preclinical or clinical supply of such Product and/or Bulk API.

In addition to the U.S. Development Plan, Takeda shall within [ \* ] after the Effective Date, draft and provide to Affymax a proposed overall plan for the Development for the Product for the Initial Indications (and each Joint Additional Indication pursued pursuant to Section 3.10, if any at that time) to support Regulatory Approval in each country of the Level 1 Markets.

**3.3 Updates to U.S. Development Plan and Development Budget.** As early as necessary in each year beginning with the first full Fiscal Year after the Effective Date, the Parties shall update and prepare the U.S. Development Plan and Development Budget for the Product for the following Fiscal Year to take into account completion, commencement or cessation of U.S. Development activities not contemplated by the then-current U.S. Development Plan, and submit such proposed U.S. Development Plan to the JSC no later than November 1 of such year, as follows: (a) Affymax, in consultation with Takeda, shall update the U.S. Development Plan for Regulatory Approval of the Product in the Renal Indications; and (b) Takeda shall update the U.S. Development Plan for Regulatory Approval of the Product in the Oncology Indications in consultation with Affymax. The JSC shall have the right to approve updates to the U.S. Development Plan and Development Budget, subject to the final decision-making authority described in Section 2.5(c) above. The JSC shall endeavor to finalize its approval of each updated U.S. Development Plan by December 15 of each year.

### **3.4 Development Expenses.**

(a) The Parties shall share any and all Development Expenses as follows: Takeda shall bear the initial fifty million Dollar (\$50,000,000) of total Development Expenses; any Development Expenses in excess of such amount shall thereafter be borne seventy percent

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(70%) by Takeda and thirty percent (30%) by Affymax. For clarity, the Development expenses incurred in connection with the ROW Development shall not be included in the Development Expenses; provided, that if the JSC determines that the Parties will use any results of the ROW Development to support the Regulatory Approval of the Product in the U.S., then, Affymax shall without delay reimburse Takeda for thirty percent (30%) of the external expenses incurred by Takeda on and after January 1, 2007 for the applicable ROW Development.

(i) Each Party shall calculate and maintain records of all relevant Development Expenses incurred by it for the Development of the Product, in accordance with procedures to be agreed upon between the Parties. The Parties understand and agree that Internal Expenses shall not be shared, subject to Section 3.4(a)(iv).

(ii) Within ten (10) Business Days following the end of each calendar quarter, Takeda shall submit to Affymax a written report setting forth in reasonable detail the Development Expenses it has incurred in such calendar quarter. Within ten (10) Business Days following the end of each calendar quarter, Affymax shall submit to Takeda a written report setting forth in reasonable detail the Development Expenses it has incurred in such calendar quarter.

(iii) Within twenty (20) Business Days following the end of each calendar quarter, Takeda shall submit to Affymax a written report setting forth in reasonable detail the detailed calculation of all Development Expenses for the Product, and the calculation of any net amount owed by Affymax to Takeda or by Takeda to Affymax, as the case may be, in order to ensure the appropriate sharing of Development Expenses in accordance with the provisions of Section 3.4(a). The net amount payable shall be paid by Takeda or Affymax to the other Party, as the case may be, within twenty-five (25) Business Days following the end of each calendar quarter; provided, that, in the event of a dispute, any amounts not in dispute shall be paid and the disputing Party shall provide written notice without undue delay after receipt of the written report in question to the other, specifying such dispute and explaining the basis of the dispute. Affymax and Takeda shall promptly thereafter meet and negotiate in good faith a resolution to such dispute and, promptly upon resolution of such dispute, the applicable Party shall make the agreed-upon payment. If such dispute is not resolved within forty-five (45) days after delivery of a notice of dispute with respect thereto to the other Party, the disputing Party may audit the other Party in accordance with the provisions of Section 8.11. For clarity, nothing in this Section 3.4(a)(iii) shall serve to limit a Party's ability to seek recourse for billing errors discovered after payment is made.

(iv) The Parties acknowledge and agree that Internal Expenses shall not be reimbursed or shared except as set forth in this Section 3.4(a)(iv). In connection with the U.S. Development, either Party may refer to the Finance Subcommittee to provide certain specified Development activities using internal resources and to include such Internal Expenses as the Development Expenses to be shared hereunder. Any such referral shall include a sufficiently detailed description of the proposed Development activities, the associated Internal Expenses, and, where possible, the costs and expenses to be paid to Third Party contractors if the same Development activities were contracted out to them. If the JSC approves (which approval shall not be unreasonably withheld) the proposal of the Finance Subcommittee to include such Internal Expenses as the Development Expenses, then the proposing Party shall obtain reimbursement as

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the Development Expenses for the Internal Expenses actually incurred (in an amount not to exceed any approved amount) in performing such Development activities for the Product.

(b) Takeda shall bear all costs and expenses associated with the ROW Development, subject to Section 3.4(a).

(c) Any reimbursement payments made pursuant to this Section 3.4 shall be subject to the general payment procedures set forth in Sections 8.7 through 8.11, inclusive.

### **3.5 Performance; Diligence.**

(a) Each Party shall devote Diligent Efforts to the U.S. Development of the Product for the Initial Indications and for any Joint Additional Indication in the U.S. consistent with the then-current U.S. Development Plan and in accordance with this Agreement.

(b) Takeda shall devote Diligent Efforts to the ROW Development of the Product for the Initial Indications and for any Joint Additional Indications for all the Level 1 Markets, and such other countries of the Royalty Territory wherein Takeda at its discretion elects to Develop the Product (as described in further detail in this Section 3.5 below), in accordance with its plan of ROW Development, the overall plan and updates of which shall be submitted to the JSC for such countries pursuant to Section 3.2.

(c) Without limiting the generality of Section 3.5(b), Takeda shall (i) devote Diligent Efforts to obtaining Regulatory Approval of the Product for the Initial Indication and for any Joint Additional Indication in the Level 1 Markets, and (ii) file for Regulatory Approval of the Product with the EMEA promptly after, but in no event more than nine (9) months after, the submission for Regulatory Approval of the Product for such indication in the U.S., unless Takeda is required to conduct any additional Development activities to comply with the EMEA's requirements. Any failure by Takeda to comply with the terms of this Section 3.5(c) shall be deemed a material breach of this Agreement by Takeda in any applicable country or countries of the Level 1 Markets, and Affymax shall have the right to terminate this Agreement with respect to the applicable country(ies) of the Level 1 Markets pursuant to the terms of Section 13.2(b)(i).

(d) Without limiting the generality of Section 3.5(b), at any time after the date of the first approval of NDA for the Product in the U.S. (for [ \* ]) of the Level 2 Markets) or the date of the first Regulatory Approval from the EMEA (for the other countries of the Level 2 Markets), Affymax may request Takeda, with regard to one or more countries of the Level 2 Markets where Takeda has not yet determined or initiated efforts to Develop and Commercialize the Product, to inform Affymax of its decision on whether or not it shall devote the Diligent Efforts to Develop and Commercialize the Product for the Initial Indication and the Joint Additional Indication, if any, in such country(ies).

(i) If Takeda informs Affymax of its decision to devote the Diligent Efforts in such country(ies), then:

(1) Takeda shall thereafter be obligated to devote Diligent Efforts in such country(ies);

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(2) Takeda shall develop a plan setting forth, for such country(ies) of the Level 2 Markets, a schedule of activities to be performed by Takeda for the filing of Regulatory Approval for the Product in each such country within [ \* ] days after such Affymax's request which period of response may be extended by Affymax's consent;

(3) Affymax shall have a right to review and comment on the plan provided by Takeda and Takeda shall consider in good faith any reasonable comments from Affymax; and

(4) in the case of failure by Takeda to comply with such Diligent Effort obligation with respect to such country(ies), Affymax shall have the right to terminate this Agreement with respect to such country(ies) pursuant to the terms of Section 13.2(b)(i).

(ii) If Takeda informs Affymax of its decision not to use such Diligent Efforts in such country(ies) or fails to provide Affymax with such a plan with respect to such country(ies) of the Level 2 Markets within the above-mentioned [ \* ] day period, or any extension thereof as agreed jointly by the Parties, then

(1) Affymax may prepare a plan it believes is commercially reasonable for both Parties to pursue for the Development and Commercialization of the Product in such country(ies) and provide it to Takeda within a reasonable time;

(2) if the Parties agree on a plan with respect to such country(ies) of the Level 2 Markets, then Takeda shall devote Diligent Efforts to obtaining Regulatory Approval of the Product for the Initial Indication and for any Joint Additional Indication in each such country(ies) under this Agreement; and

(3) if Affymax informs Takeda of its intention not to provide such plan as mentioned in Section 3.5(d)(ii)(1), or, both Parties cannot agree on such plan within [ \* ] days after Takeda's receipt of such plan, then such country(ies) shall thereafter be excluded from the Licensed Territory and Affymax shall thereafter have a right, with a right to sublicense to Third Parties, to Develop and Commercialize the Product for the applicable Initial Indications or Joint Additional Indications, if any, in such country(ies) by using the Takeda Technology and the Regulatory Materials without any consideration to Takeda.

(e) With respect to any country in the Royalty Territory other than the Level 1 Markets and Level 2 Markets, Takeda shall have the discretion to decide whether and to what extent to Develop, seek Regulatory Approval for, and Commercialize the Product.

(f) Each Party shall conduct its Development activities under this Agreement in good scientific manner and in compliance in all material respects with all applicable Laws, including without limitation applicable GCP, GLP, and GMP.

**3.6 Records, Reports and Information.** Each Party shall maintain complete, current and accurate records of all work conducted by it under the U.S. Development Plan and all data and other Information resulting from such work. Such records shall fully and properly reflect all

work done and results achieved in the performance of the U.S. Development Plan in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes. Each Party shall have the right to review such records maintained by the other Party at reasonable times, upon written request. Each Party shall provide written reports in English to the JSC on its Development and regulatory activities with the Product pursuant to the U.S. Development Plan on a quarterly basis at the end of each calendar quarter, at a level of detail reasonably sufficient to enable the other Party to determine the reporting Party's compliance with its Diligent Efforts obligation pursuant to Section 3.5.

**3.7 Backup Research Agreement.** Promptly after the Effective Date, the Parties shall negotiate in good faith a research agreement setting forth the terms and conditions under which Affymax shall perform a program of research intended to [ \* ] for the Initial Indications. Such research agreement (the "**Backup Research Agreement**"), if concluded, shall provide that Takeda shall bear the costs and expenses of such research program in an amount not to exceed [ \* ] per year. For the avoidance of doubt, the failure of the Parties to enter into the Backup Research Agreement shall not constitute a breach of this Agreement by either Party.

### **3.8 Replacement Products.**

(a) In the event that Takeda discontinues its Development of the Product in its entirety within the period commencing on the Effective Date and ending [ \* ] years thereafter due to patient safety concerns or pursuant to a requirement imposed by Regulatory Authorities in the Licensed Territory or by the external monitoring board or upon mutual agreement of the Parties, then Takeda shall have the right to review with Affymax any and all then-existing Replacement Product Candidates and to select within [ \* ], jointly with Affymax, one such Replacement Product Candidate as a substitute for the then-current Product and to initiate and conduct a Development for such Replacement Product Candidate. In such event, products containing such Replacement Product Candidate shall be included in the definition of the "Product" for purposes of this Agreement (including without limitation, with respect to all relevant payment including the various milestone payments described in Section 8.2, but only to the extent that any such payment was not previously made for the discontinued Product and other obligations, and the licenses set forth in Article 6). In connection with such substitution, the U.S. Development Plan for the Product shall be amended to reflect the substitution of the replacement Product in a manner that is mutually acceptable to each Party (it being understood that the Parties shall retain the respective rights and obligations with respect to the Development and Commercialization of such Replacement Product Candidate in accordance with the terms of this Agreement).

(b) If, in the case of Section 3.8(a) above, the Parties fail to agree on the Replacement Product Candidate to take its place within above-mentioned period of [ \* ], then Takeda may elect to proceed with the Replacement Product Candidate of its choice pursuant to the terms of Section 3.8(a) above, except that, notwithstanding anything to the contrary in this Agreement: (i) Takeda shall bear all responsibilities and costs associated with the Development and Commercialization of such Product throughout the Licensed Territory, (ii) Affymax shall have no co-promotion right with respect to such replaced Product in the U.S., (iii) the U.S. shall be deemed part of the Royalty Territory, except that the royalties applicable to sale of thus replaced Product in the Royalty Territory (including U.S.) shall be as set forth in Exhibit O rather

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than in Section 8.5(a), and (iv) Takeda shall make the various milestone payments described in Section 8.2, but only to the extent that any such payment was not previously made for the discontinued Product.

(c) Notwithstanding the foregoing, Takeda acknowledges and understands that any Replacement Product Candidate may not have been manufactured at scale, or may not have been the subject of sufficient Development or any manufacturing process development, or may not be the subject of any manufacturing agreement in place at such time between Affymax and its third party manufacturers, in each case at the time of the selection of such Replacement Product Candidate, and accordingly, that such product development, manufacturing process development and scale up activities may need to be conducted by Takeda, alone or in conjunction with Affymax, as agreed upon by Takeda and Affymax, and that such Replacement Product Candidate may be subject to Third Party patent rights which may require the acquisition of additional Third Party licenses prior to commercialization (which such licenses shall be treated in accordance with Section 6.7(b)). Subject to the terms of Section 3.9 and to the exclusivity covenant set forth in Section 6.6, after the expiration of the time period described above in Section 3.8(a), Affymax shall have the right to pursue any Replacement Product Candidate not selected by Takeda pursuant to Section 3.8(b), itself or with an Affiliate or Third Party, without any further obligation to Takeda.

**3.9 Right of First Negotiation to Backup Compounds.** If, within [ \* ] years after the Effective Date, Affymax develops one or more potential Backup Compounds, then Takeda shall have a right of first negotiation to develop and commercialize such Backup Compound(s) for the Licensed Territory as provided in this Section 3.9. During such [ \* ]-year period, Affymax shall provide Takeda on an annual basis a report stating the results of any pre-clinical and clinical studies conducted for such a Backup Compound for the prevention, treatment or amelioration of anemia in humans, as well as all other material results and data with respect to such potential Backup Compound(s), for Takeda's evaluation. Takeda shall treat such results and data as Affymax's Confidential Information under this Agreement. Takeda may elect to exercise its right with respect to a particular Backup Compound by written notice to Affymax during the [ \* ] period following Takeda's receipt of an annual report or upon the request of Affymax delivered after the completion of the initial Phase I Clinical Trial for such Backup Compound. If Takeda notifies Affymax within such period of its desire to obtain such rights, then Affymax and Takeda shall negotiate in good faith, for up to [ \* ], the terms and conditions under which Takeda may obtain such rights. If Takeda and Affymax enter into an agreement under which Takeda obtains such rights with respect to certain Backup Compound(s), then such Backup Compound(s) shall also be licensed to Takeda under such agreed terms and conditions. If Takeda fails to notify Affymax of its desire to obtain such rights within the [ \* ] notice period, or if the Parties, despite good faith negotiation, do not enter into an agreement governing the terms and conditions under which Takeda may obtain such rights from Affymax within the [ \* ] negotiation period, then, unless the Parties agree in writing to extend such period, Affymax shall have the right to pursue such opportunity itself or with an Affiliate or Third Party without any further obligation to Takeda, subject to the parallel programs limitations set forth in Section 6.6(b). This Section 3.9 shall apply on a Backup Compound-by-Backup Compound basis. For clarity, if and so far as a Backup Compound is developed by or on behalf of Affymax, then,

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subject to Affymax's obligation under Section 6.6(b), Takeda shall have no rights under this Section 3.9 with respect to such Backup Compound.

### **3.10 Additional Indications.**

(a) **Proposal.** Either Party may submit to the JSC a proposal to conduct joint Development on the Product for any specific Additional Indication. Such proposal shall outline the rationale for Developing and Commercializing the Product for the particular proposed Additional Indication and the Development activities proposed to be conducted with respect to such Additional Indication. The JSC shall promptly consider such proposal and determine whether to proceed under this Agreement to conduct such Development and Commercialization for such proposed Additional Indication.

(b) **Joint Development.** If the JSC elects to proceed pursuant to a unanimous decision, the JSC shall amend the U.S. Development Plan to include the Development activities to be conducted for such Additional Indication (a "**Joint Additional Indication**") up through Regulatory Approval in the U.S. Unless otherwise agreed by the Parties, the U.S. Development Expenses for such Development of the Product for the Joint Additional Indication shall be deemed Development Expenses.

(c) **Rejection; Failure to Agree.** If the JSC elects not to proceed with collaborative Development of the Additional Indication that was the subject of a Party's proposal, or if the JSC cannot reach a decision on such proposal within [ \* ] days of the Party's submitting the proposal, then neither Party shall be entitled to directly or indirectly proceed with the Development and/or Commercialization of the Product for such Additional Indication in the Licensed Territory, and, notwithstanding anything to the contrary contained herein, even if the JSC fails to reach unanimous decision to proceed with the Development and/or Commercialization of the Product in the Licensed Territory, such dispute shall not be subject to the procedures described in Exhibit M.

### **3.11 Manufacturing Development.**

(a) **Duties.** Affymax shall be responsible for the Manufacturing Development for Bulk API, itself or through a Third Party contract manufacturer. Takeda shall be responsible for the Manufacturing Development for the Finished Manufacture, itself or through a Third Party contract manufacturer. Affymax shall reasonably cooperate with Takeda for such purposes, which cooperation shall include the transfer to Takeda of technology Controlled by Affymax relating to activities that were conducted by Affymax as of the Effective Date and thereafter, if any, with respect to any such Finished Manufacture.

(b) **Costs.** Manufacturing Development Expenses are included in Development Expenses and, as a result, shall be shared pursuant to Section 3.4 to the extent that such Manufacturing Development Expenses relate to the Manufacturing Development for Bulk API and/or Product to be Developed and Commercialized hereunder.

(c) **Comparator Drugs.** Each Party conducting clinical trials for the Product shall be responsible for procuring all of its requirements of all comparator drugs or placebos

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necessary for conducting such clinical trials; provided, however, Affymax shall reasonably cooperate with Takeda for such purposes, which cooperation shall include the transfer to Takeda of technology Controlled by Affymax relating to activities that were conducted by Affymax as of the Effective Date with respect to any such placebo, in connection with the Development of the Product. The costs and expenses incurred by either Party for procuring the comparator drugs or placebos for the U.S. Development shall be included in the Development Expenses.

**3.12 [ \* ] and [ \* ] Development.** Affymax shall have the right unilaterally to develop and test [ \* ] containing the Peptide and/or [ \* ] (an “**Additional Product**”). Affymax shall conduct such development activities pursuant to a development plan to be provided by Affymax to Takeda after the Effective Date for Takeda’s review and comment. Affymax shall conduct such development work at its sole expense and shall have sole control over such work. Affymax shall keep Takeda informed as to progress on, results of, and expenses of Affymax for the research and development of each Additional Product with quarterly reports up through completion of the establishment of the [ \* ] on the Additional Product for any Initial Indication (including, without limitation, by providing at least [ \* ] notice of any anticipated IND filing). If Affymax reasonably believes based on objective information that [ \* ] has been established, Affymax shall provide Takeda with all then-available data relating to the Additional Product. At any time up to and including the date [ \* ] after Takeda’s receipt of such data and results up to the [ \* ] from Affymax, Takeda shall be entitled to elect to include the Additional Product into the Products under this Agreement. If Takeda exercises such right, then, without the need for further action by the Parties, the Additional Product shall thereafter be deemed to be included in the Products hereunder (in which case all obligations of the Parties under this Agreement shall apply to such Additional Product, including without limitation the obligation to share future Development Expenses, and, for clarity, Takeda shall not be obligated to make any milestone payments under Section 8.2 more than once for the Products (i.e., the Products after such inclusion of the Additional Product)); and, the Parties shall jointly create a U.S. Development Plan for such Additional Product. In connection with such exercise, Takeda shall be required to pay Affymax an amount equal to a percentage of all actual expenses incurred by Affymax (including Internal Expenses) for the performance of such independent development activities from the Effective Date up to the date of the option exercise, as follows: (a) if Takeda exercises such right within [ \* ] after the Effective Date, then Takeda shall pay [ \* ] of such expenses, (b) if Takeda exercises such right after such [ \* ] period but prior to [ \* ] any Initial Indication, Takeda shall pay [ \* ] of such expenses, (c) if Takeda exercises such right after the [ \* ] but prior to [ \* ] Initial Indication, Takeda shall pay [ \* ] of such expenses, and (d) if Takeda exercises such right after the [ \* ] Initial Indication which exercise right shall expire if not exercised within [ \* ] of [ \* ] by Affymax, Takeda shall pay [ \* ] of such expenses; provided, in each case, that Affymax shall provide Takeda with documentary evidence demonstrating the accuracy of such expenses, that the Internal Expenses among such expenses shall be calculated appropriately in consistent with Affymax’s standard accounting principal and procedures, and that Section 8.11 shall also apply with regard to such expenses. If Takeda does not exercise such right within the period described above, then, notwithstanding the limitations set forth in Section 6.6, Affymax shall have the right to Develop and Commercialize the Additional Product in any indications without any financial or other obligation to Takeda resulting in connection with such Development and Commercialization. As used in this Section 3.12, [ \* ] means indication of a product’s [ \* ] the Initial Indications to [ \* ] clinical trials.

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## ARTICLE 4

### REGULATORY MATTERS

#### 4.1 Transfer of Data and Regulatory Materials.

(a) **Existing Data.** Within [ \* ] after the Effective Date, Affymax shall provide Takeda with copies of IND and CTA submissions made for the Product in the U.S. and EU prior to the Effective Date, unless previously provided. With regard to all other preclinical and non-clinical data relevant to an IND or CTA submission (including, as needed for Takeda regulatory submissions, copies of [ \* ] the above-mentioned IND and CTA submissions, in the form then existing) generated as of the Effective Date and Controlled by Affymax, Affymax shall, if requested by Takeda, provide Takeda with copies thereof within a reasonable time after such request to the extent relevant to the Development of Product or Takeda's seeking Regulatory Approval for the Product in the Field in the Licensed Territory. Takeda shall have the full right, without any additional consideration, to use any and all such data and reports supplied by Affymax under this Section 4.1(a) in connection with the Development and/or Commercialization of the Product in the Licensed Territory, including the incorporation of such data or reports in any regulatory submissions, including MAA and NDA submissions.

(b) **Future Data.** Each Party shall, in a timely manner and compliant with requirements of the FDA, the EMEA, and any other applicable Regulatory Authority, provide the other Party with copies of all preclinical, non-clinical, analytical, manufacturing, and clinical data relating to the Product, generated by or on behalf of such Party in connection with the performance of the U.S. Development Plan and relevant to any regulatory submission; provided, that information regarding adverse events and serious adverse events shall be provided promptly as set forth in Section 4.8. If the receiving Party requests that copies of such data be provided in compliance with requirements of other Regulatory Authorities, the disclosing Party shall reasonably consider such request. Affymax shall have the full right, without any additional consideration, to use any and all such data and reports in connection with the Development of the Product in the Licensed Territory and/or in connection with the Commercialization of the Product in the U.S., and, Takeda shall have the full right, without any additional consideration, to use any and all such data and reports in connection with the Development and/or the Commercialization of the Product in the Licensed Territory, including the incorporation of such data or reports in any regulatory submissions including MAA and/or NDA submissions.

(c) **Clarification.** All preclinical, non-clinical, analytical, manufacturing, and clinical data and associated reports disclosed by one Party to the other under this Agreement shall be deemed Confidential Information of the disclosing Party. Except as otherwise provided in this Section 4.1, the receiving Party may use such data solely for the purpose of developing the Product, seeking and obtaining Regulatory Approval and Commercializing the Product as permitted in this Agreement, subject to Article 12.

#### 4.2 Regulatory Submissions and Approvals.

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**(a) In General.** The Parties intend that the U.S. Development Plan shall set forth the regulatory strategy approved by the JSC. The Parties intend to seek Regulatory Approval in the first instance in the U.S. and EU and thereafter the remainder of the Licensed Territory wherein Takeda Develops and Commercializes the Product. The Parties also intend that each Party with responsibility for generating data will cooperate fully with the other Party to make that data available for preparation and submission of Regulatory Materials. Subject to the terms of this Article 4:

**(i)** In the U.S., Affymax, in consultation with Takeda, shall be responsible for assembling, submitting and maintaining any source regulatory submission components and compiled submissions of the Regulatory Materials to be used in support of Regulatory Approval for the Product in the U.S. in accordance with such regulatory strategy, including without limitation NDAs and associated documents;

**(1)** Affymax shall have primary responsibility for providing components of Regulatory Materials relating to Bulk API and Takeda shall have primary responsibility of providing components of Regulatory Materials relating to Finished Product in support of Regulatory Approval;

**(2)** Affymax shall have primary responsibility for providing the content of Regulatory Materials relating to clinical data supporting Regulatory Approval of Renal Indications. Takeda shall have primary responsibility for providing the content of Regulatory Materials relating to clinical data supporting Regulatory Approval of the Oncology Indications;

**(ii)** In the Royalty Territory, Takeda, in consultation with Affymax as set forth in Section 4.4(a), shall be responsible for assembling, submitting and maintaining any source regulatory submission components and compiled submissions of the Regulatory Materials to be used in support of Regulatory Approval for the Product in the Royalty Territory including without limitation MAAs and associated documents;

**(1)** Affymax shall have primary responsibility for providing components of Regulatory Materials relating to Bulk API and Takeda primary responsibility of providing components of Regulatory Materials relating to Finished Product in support of Regulatory Approval;

**(2)** Affymax shall have primary responsibility for providing the content of Regulatory Materials relating to clinical data supporting Regulatory Approval of Renal Indications. Takeda shall have primary responsibility for providing the content of Regulatory Materials relating to clinical data supporting Regulatory Approval of the Oncology Indications;

**(iii)** Affymax, in consultation with Takeda, shall be primarily responsible for preparing and submitting to Regulatory Authorities INDs, CTAs and all associated submissions (e.g., IMPDs, safety alerts, protocol submissions, etc.) for the Renal Indications for the Product and for carrying out clinical protocols in support of Regulatory Approval in the U.S. and contained in the U.S. Development Plan under said INDs and CTAs in

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both the U.S. and in the Royalty Territory in accordance with such regulatory strategy. Takeda, in consultation with Affymax, shall be primarily responsible for carrying out clinical protocols not contained in the U.S. Development Plan but specifically required by relevant Regulatory Authorities in the Royalty Territory, to support Regulatory Approval for the Renal Indications for the Product in the Royalty Territory, in which case, Takeda may decide whether to newly prepare and submit CTAs for carrying out such clinical protocols by itself or to use Affymax's existing CTAs, if any, for carrying out such protocol in the Royalty Territory, and, Affymax shall, if requested by Takeda, fully cooperate with Takeda in Takeda's carrying out such protocols;

(iv) Takeda, in consultation with Affymax, shall be primarily responsible for preparing and submitting to Regulatory Authorities INDs and CTAs and all associated submissions (*e.g.*, IMPDs, safety alerts, protocol submissions, etc.) for the Oncology Indications for the Product and for carrying out clinical protocols under said INDs and CTAs, in both the U.S. and in the Royalty Territory in accordance with such regulatory strategy. Affymax shall, as soon as possible after the Effective Date, free of charge arrange for transfer to Takeda ownership of all the INDs and CTAs for the Oncology Indications for the Product in the EU and in the U.S. made by Affymax on or before the Effective Date.

(b) **Costs and Expenses.** Any Development Expenses to the extent required for the Parties to prepare, submit and maintain all Regulatory Materials in the U.S. (including any materials that are intended for submission to Regulatory Authorities in both the U.S. and Royalty Territory) shall be treated as U.S. Development Expenses. Unless otherwise provided for in this Agreement, any efforts, costs and expenses for the ROW Development shall be borne solely by Takeda and not treated as U.S. Development Expenses.

(c) **Rights of Reference to Regulatory Materials.** Each Party hereby grants to the other Party a right of reference to all Regulatory Materials filed by such Party for Product as follows: The right of reference granted to Affymax herein shall be solely for the purpose of Affymax obtaining Regulatory Approval for the Product in the U.S. The right of reference granted to Takeda herein shall be solely for the purpose of obtaining Regulatory Approval for the Product in the Field in the Royalty Territory, and/or, if necessary or applicable, for the purpose of fulfilling its responsibility in relation to the Regulatory Approval for the Product for the Oncology Indications in U.S. Each Party shall refer the Regulatory Materials filed by the other Party for Product as feasible (*e.g.*, for avoiding redundancy of work as far as possible). Takeda also shall have a right to use, without any additional consideration, any and all data and information generated or obtained from either Party hereunder, for the purpose of Takeda's Development and Commercialization of the Product in Japan under the Japan Agreement.

#### **4.3 Affymax's Rights and Obligations.**

(a) **Preparation.** Affymax shall prepare and author all Renal Indication documents and build, submit and maintain any Regulatory Materials for Regulatory Approval of the Product in the U.S., in accordance with the regulatory strategy approved as a component of the U.S. Development Plan by the JSC.

(b) **Compliance.** Affymax shall comply with applicable Laws and other regulatory obligations related to the submission and maintenance of any Regulatory Materials for Regulatory Approval of the Product in the U.S. (including the submission of Marketing Materials to the Regulatory Authorities).

(c) **Meetings.** Affymax shall request the FDA or other applicable Regulatory Authority in the U.S. to allow a reasonable number of Takeda representatives to attend and, to the extent permitted under applicable law, participate in all meetings between Affymax and such Regulatory Authority in respect of any Regulatory Materials pertaining to each of the Renal Indications before and following NDA approval and to each of the Oncology Indications following NDA approval, on an Regulatory Approval by Regulatory Approval basis (it being understood that Affymax shall be the official sponsoring company with respect to such meetings). Notwithstanding the foregoing, the Parties agree that, to the extent permitted under applicable law, Affymax shall be the primary presenter and responder regarding the Renal Indications and Takeda shall be the primary presenter and responder with regard to Oncology Indications, unless otherwise agreed upon by the Parties beforehand. Affymax shall timely inform Takeda of any such meetings scheduled with such Regulatory Authority in respect of any Regulatory Materials as soon as practically possible.

(d) **Ownership.** Except as otherwise expressly agreed by the Parties, for so long as Affymax owns Regulatory Materials under this Section 4.3(d), any Regulatory Materials for Regulatory Approval of the Product in the U.S. (except for the INDs for Oncology Indications, which shall be owned by Takeda pursuant to Section 4.4(c)) shall be held in Affymax's name and shall be owned solely by Affymax, subject to Takeda's rights under Section 4.2(c) of this Agreement.

#### **4.4 Takeda Rights and Obligations.**

(a) **Preparation.** Takeda shall prepare and author all Oncology Indications documents for Regulatory Approval of the Product in the U.S. Takeda shall prepare and author all MAA-related documents for all indications and build, submit and maintain Regulatory Materials in countries of the Royalty Territory wherein Takeda Develops and Commercializes the Product and seek Regulatory Approval for the Product in such countries of the Royalty Territory, in consultation with Affymax if necessary, for the purpose of coordinating U.S. and Royalty Territory filing content including any activities relating to country-specific clinical trials; provided, that Affymax shall have a right of consent (subject to final resolution in accordance with Exhibit M in the case of an unresolved disagreement between the Parties) with respect to the content of any Regulatory Materials in the Royalty Territory that are reasonably expected to create a serious material adverse effect on the U.S. Development, Regulatory Approval, or Commercialization of the Product in the U.S. As part of the foregoing, Takeda shall be responsible for seeking any necessary approvals of Regulatory Authorities in such countries of the Royalty Territory for Product Labeling and Promotional Materials to be used in the applicable jurisdiction(s) in connection with Commercializing the Product. Upon the request of Affymax, where permitted, Takeda shall request the Regulatory Authority in a particular country or territory of the Royalty Territory to allow at least one Affymax representative to attend, and, upon the request of Takeda and where permitted, Affymax shall make at least one Affymax representative to attend, as a silent observer (unless otherwise agreed in advance by the

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Parties), all meetings between Takeda and such Regulatory Authority in the Royalty Territory, and Takeda shall timely inform Affymax of any such meetings scheduled with the Regulatory Authority in the Royalty Territory as soon as practically possible.

(b) **Compliance.** Takeda shall comply with applicable Laws and other regulatory obligations related to Product Development and Regulatory Approval submission made by it in the Licensed Territory (including the submission of Marketing Materials to the Regulatory Authorities).

(c) **Ownership.** Any Regulatory Materials in the Royalty Territory and INDs for the Oncology Indication is the U.S. (including those transferred to Takeda from Affymax pursuant to Section 4.2.(a)(iv)) shall be held in Takeda's name and shall be owned solely by Takeda, subject to Affymax's rights under Section 4.2(c) of this Agreement.

(d) **Meetings.** Takeda shall request the FDA or other applicable Regulatory Authority in the U.S. to allow a reasonable number of Affymax representatives to attend and, to the extent permitted under applicable law, participate in all meetings between Takeda and such Regulatory Authority in respect of any Regulatory Materials pertaining to the Oncology Indications before NDA approval (it being understood that Takeda shall be the official sponsoring company with respect to such meetings). It is understood and agreed that, to the extent permitted under applicable law, Takeda shall be the primary presenter and responder with regard to Oncology Indications, unless otherwise agreed upon by the Parties beforehand. Takeda shall timely inform Affymax of any such meetings scheduled with such Regulatory Authority in respect of any Regulatory Materials as soon as practically possible.

#### **4.5 Consultation, Reporting and Review.**

(a) Each Party shall keep the other Party reasonably and regularly informed of, the status of the preparation of all Regulatory Materials, Regulatory Authority review of Regulatory Materials, and Regulatory Approvals made by it for the Product in the U.S. and EU and will give reasonable consideration to any comments received from such other Party with respect to such Regulatory Materials.

(b) Each Party shall provide the other Party, in a timely manner, with copies of all Regulatory Approvals it receives for the Product.

(c) Each Party shall provide the other Party, in a timely manner, with copies of, and all information received by it pertaining to, notices, questions, actions and requests from or by Regulatory Authorities in the Licensed Territory with respect to the Product, the Peptide, [ \* ] or Hematide, or the testing, manufacture, distribution or facilities in relation thereto, including without limitation any notices of non-compliance with Laws in connection with the Product (e.g., warning letters or other notices of alleged non-compliance), audit notices, notices of initiation by Regulatory Authorities of investigations, inspections, detentions, seizures or injunctions concerning the Product (or its manufacture, distribution, or facilities connected thereto), notice of violation letters (i.e., an untitled letter), warning letters, service of process or other inquiries.

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**4.6 Communications.** Except as may be required by Laws, only the Party that holds the IND, CTA, NDA, MAA, etc. in a particular country or territory shall communicate regarding the Product with any Regulatory Authority having jurisdiction in such country or territory. However, responses to a regulatory request or inquiry of a substantial nature, such as would impact regulatory or development strategy, requires consultation with the other Party prior to the communication and, whenever possible, include participation by the other Party. If the Party not holding the IND, CTA, NDA, MAA, etc. is required to make such a communication by a Regulatory Authority in the Licensed Territory, then such Party shall provide immediately to the other Party notice of such order.

**4.7 Adverse Event Reporting and Safety Data Exchange.** The Parties agree that Takeda shall be responsible for the establishment of the global safety database for the Product in the Licensed Territory and the monitoring of all clinical experiences and submission of all required reports throughout clinical Development and Commercialization of the Product in the Royalty Territory, and that Affymax shall have primary responsibility for the monitoring of all clinical experiences and submission of all required reports concerning the Product in the U.S., provided, however, that Takeda shall have primary responsibility for monitoring all clinical experiences for the Oncology Indications. Specific details regarding the exchange and management of information relating to adverse events related to the use of the Product shall be delineated in a separate agreement that shall be agreed to by the Parties within [ \* ] after the Effective Date. The pharmacovigilance and product labeling personnel of each Party shall work in good faith together during such time to negotiate an agreement, consistent with each Party's current standard operating procedures and, to the extent practical, with the then-current agreements between the Parties, that:

- (a) identifies which safety information shall be exchanged;
- (b) identifies when such information shall be exchanged;
- (c) provides that Takeda shall have regulatory reporting responsibilities concerning the Product in the Royalty Territory, and that Affymax shall have such responsibilities concerning the Product in the U.S. (in each case, either itself or through a clinical research organization with which it has contracted);
- (d) provides that Takeda shall manage the global safety database;
- (e) identifies which Party shall be obligated to obtain follow-up information on incomplete safety reports;
- (f) identifies which Party shall review the literature for safety report information;
- (g) sets forth the roles and responsibilities of the Parties related to review and approval of safety information for inclusion in the Product Labeling in the Licensed Territory;
- (h) sets forth standard operating procedures to be implemented by the Parties in their reporting of safety and other pharmacovigilance information;

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(i) sets forth provisions governing access to safety information and coordination with regard to information reporting to the applicable Regulatory Authorities;

(j) identifies which Party shall prepare required periodic safety updates; and

(k) identifies any other details required to appropriately manage safety information for the Product, the Peptide, [ \* ] or Hematide.

**4.8 Regulatory Authority Communications Received by a Party.** Each Party shall keep the other Party informed, in a timely manner and in any event in compliance with the reporting requirements of Regulatory Authorities in the Licensed Territory, of notification of any action by, or notification or other information which the first Party receives (directly or indirectly) from any such Regulatory Authority which: (a) raises any [ \* ] of the Product; (b) indicates or suggests [ \* ] in connection with the Product; (c) is reasonably likely to lead to [ \* ] of the Product; or (d) relates to [ \* ] with respect to the Product, or [ \* ], and which may have [ \* ] the Product, the Peptide, [ \* ] or Hematide. The Party identified in 4.2(a) as being responsible for preparing and authoring the content of documents and components of regulatory submissions shall be responsible for preparing the response to the communication, and the Party identified as being responsible for building, submitting and maintaining submission components will submit the response. However, before submitting such response to a Regulatory Authority regarding the communication, the submitting Party shall have an opportunity to comment on the response. In the event the Parties disagree concerning the form or content of a response to a Regulatory Authority in a particular country of the Licensed Territory, the Party who has responsibility for content preparation shall decide the appropriate form and content of such response, without recourse to arbitration under Section 2.4(c). The other Party shall fully cooperate with and assist such Party in complying with such regulatory obligations and communications, including by providing to such Party, within two (2) Business Days after a request or as quickly as practicable thereafter, such information and documentation in the other Party's possession as may be necessary or helpful for the Party to prepare a response to an inquiry from a Regulatory Authority. For clarity, each Party's obligations under this Section 4.8 shall apply to any such communications regarding the matters referred to above received by such Party's Affiliate(s), contractors, partners, or other collaborators as if such communications had been received by such Party directly.

#### **4.9 Regulatory Inspection or Audit.**

##### **(a) Audit of Takeda.**

(i) If a Regulatory Authority in the U.S. desires to conduct an inspection or audit with regard to the Product of Takeda's facility or a facility under contract with Takeda in or for the U.S., Affymax shall promptly notify Takeda. In such case, Takeda shall permit and cooperate with such inspection or audit, and shall cause the contract facility to permit and cooperate with such Regulatory Authority and Affymax during such inspection or audit. Affymax shall have the right to have a representative observe such inspection or audit and Affymax shall, if requested by Takeda, assist Takeda in preparing for, facilitating or enabling such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which Affymax shall immediately provide to Takeda), Takeda

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shall prepare a draft response to any such observations in English, in consultation with Affymax, and Affymax shall prepare and file the final response with such Regulatory Authority in the U.S.

(ii) If a Regulatory Authority in the Royalty Territory desires to conduct an inspection or audit with regard to the Product of Takeda's facility or a facility under contract with Takeda in or for the Royalty Territory, Takeda shall promptly notify Affymax. In such case, Takeda shall permit and cooperate with such inspection or audit, and shall cause the contract facility to permit and cooperate with such Regulatory Authority during such inspection or audit. Affymax shall have the right to have a representative observe such inspection or audit and Affymax shall, if requested by Takeda, assist Takeda in preparing for, facilitating or enabling such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which Takeda shall immediately provide to Affymax), Takeda shall prepare and file the final response with such Regulatory Authority, and shall provide a copy of such response to Affymax.

**(b) Audit of Affymax.**

(i) If a Regulatory Authority in the U.S. desires to conduct an inspection or audit of Affymax's facility, or a facility under contract with Affymax, with regard to the Product or the Bulk API in or for the U.S., Affymax shall promptly notify Takeda and permit and cooperate with such inspection or audit, and shall cause the contract facility to permit and cooperate with such Regulatory Authority during such inspection or audit. Takeda shall have the right to have a representative observe such inspection or audit and Takeda shall, if requested by Affymax, assist Affymax in preparing for, facilitating or enabling such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which Affymax shall immediately provide to Takeda), Affymax shall prepare a draft response to any such observations in English, in consultation with Takeda, and Affymax shall prepare and file the final response with such Regulatory Authority, and shall provide a copy of such response to Takeda.

(ii) If a Regulatory Authority in the Royalty Territory desires to conduct an inspection or audit of Affymax's facility, or a facility under contract with Affymax, with regard to the Product or the Bulk API in or for the Royalty Territory, Takeda shall promptly notify Affymax. In such a case, Affymax shall permit and cooperate with such inspection or audit, and shall cause the contract facility to permit and cooperate with such Regulatory Authority and Takeda during such inspection or audit. Takeda shall have the right to have a representative observe such inspection or audit and Takeda shall, if requested by Affymax, assist Affymax in preparing for, facilitating or enabling such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which Takeda shall immediately provide to Affymax), Affymax shall prepare a draft response to any such observations in English, in consultation with Takeda, and Takeda shall prepare and file the final response with such Regulatory Authority, and shall provide a copy of such response to Affymax.

**(c) Audit Procedures.** In any event, each Party shall notify the other Party within [ \* ] of receipt of notification from a Regulatory Authority of the intention of such Regulatory Authority to audit or inspect facilities being used to conduct manufacture of Bulk API or Finished Manufacture of the Finished Product. Each Party shall also provide the other

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Party with copies of any written communications received from Regulatory Authorities with respect to such facilities within [ \* ] of receipt.

**4.10 Recalls and Voluntary Withdrawals.** The Parties shall exchange and provide timely updates to their internal standard operating procedures (“SOPs”) for conducting product recalls reasonably in advance of the First Commercial Sale of any Product in the Licensed Territory, and shall discuss and resolve any conflicts between such SOPs and issues relating thereto promptly after such exchange. If either Party becomes aware of information relating to any Product that indicates that a unit or batch of Finished Product or Bulk API may not conform to the specifications therefor, or that potential adulteration, misbranding, or other issues have arisen that relate to the safety or efficacy of the Product, it shall promptly so notify the other Party. The JSC shall meet to discuss such circumstances and to consider and decide appropriate courses of action, which shall be consistent with the internal SOP of Takeda. The Party that holds the applicable Regulatory Approval shall have the right and responsibility to control any product recall, field correction, or withdrawal of any Product in the Licensed Territory that is required by Regulatory Authorities in the Licensed Territory, and the allocation of expenses incurred in connection with such recall between the Parties shall be made as follows: (i) if the recall is due to manufacturing defect (in accordance with then prevailing U.S. product liability Laws, unless otherwise agreed upon by the Parties in the Supply Agreement) of Bulk API, then Affymax shall bear all such expenses, (ii) if the recall is due to manufacturing defect (in accordance with then prevailing U.S. product liability Laws, unless otherwise agreed upon by the Parties in the Supply Agreement) of Finished Product (other than due to manufacturing defect of Bulk API), then Takeda shall bear all such expenses, (iii) if the recall is due to both of (i) and (ii), then the Parties shall share all such expenses proportionately and (iv) otherwise, as follows: (1) 100% to Takeda to the extent attributable to a recall in any country in the Royalty Territory; (2) treated as Commercial Expenses to the extent attributable to a recall in the U.S., or (3) or as otherwise may be agreed for one or more territories in the Supply Agreement as described in Section 7.3. In addition, Takeda shall have the right, at its discretion, to conduct any product recall, field correction or withdrawal of any Product in the Licensed Territory that is not so required by such Regulatory Authorities but that Takeda deems to be appropriate, and the allocation of expenses incurred in connection with such recall between the Parties shall be as set forth in the immediately preceding sentence. Takeda shall maintain complete and accurate records of any recall in the Licensed Territory for such periods as may be required by applicable Laws, but no event for less than three (3) years.

## **ARTICLE 5**

### **COMMERCIALIZATION**

#### **5.1 Commercialization in the Licensed Territory.**

(a) **U.S. Territory.** Takeda and Affymax shall have the rights and responsibilities for Commercializing the Product in the U.S. in the Field in accordance with the U.S. Commercialization Plan for the Product, as provided in this Article 5; provided, however, that, during the Co-Promotion Term, the terms of the Co-Promotion Agreement (as defined in Section 5.7) shall apply to the Parties’ co-promotion of the Product in the U.S. Takeda shall book all sales of the Product in the U.S. The Parties shall share equally all Commercial

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Expenses incurred by the Parties in connection with such Commercialization in the U.S. in accordance with the procedures described in Section 8.4.

**(b) Royalty Territory.** Takeda shall have sole right and responsibility for Commercializing the Product in the Royalty Territory in the Field, as provided in this Article 5. Takeda shall book all sales of the Product in the Royalty Territory and shall bear all of the costs and expenses incurred in connection with such Commercialization in the Royalty Territory except as expressly provided for herein. Takeda may use sublicensees to Commercialize the Product in the Royalty Territory in the Field, subject to Affymax's approval right described in Section 6.1. Subject to Takeda's diligence obligations in Section 3.5, Takeda is entitled to decide, at its discretion, on whether and in which countries of the Royalty Territory other than the Level 1 Markets it would pursue Development and Commercialization of the Product.

## **5.2 Commercialization Plans.**

**(a) For the U.S.** The strategy for the commercial launch of the Product in the U.S. shall be described in a comprehensive plan that describes the pre-launch, launch and subsequent Commercialization activities and budget for the Product (including, if available, advertising, education, planning, marketing, sales force training and allocation, distribution, pricing, and reimbursement) (the "**U.S. Commercialization Plan**"). The JSC shall establish appropriate subcommittee(s) at least thirty-six (36) months prior to the then-current date of expected Regulatory Approval for such Product in the U.S. in the Field as determined in accordance with then-current U.S. Development Plan (such date, the "**U.S. Approval Date**"). The JSC and its subcommittees shall develop and approve an initial U.S. Commercialization Plan at least twenty-four (24) months prior to the U.S. Approval Date. The initial U.S. Commercialization Plan and subsequent revisions thereto, which revisions shall be approved by the JSC from time to time, shall contain such information as the JSC believes necessary for the successful commercial launch of such Product in the U.S. in the Field in each of the Initial Indications and shall generally conform to the level of detail utilized by the Parties in preparation of their own product commercialization plans. The U.S. Commercialization Plan shall be deemed Confidential Information of both Parties, and each Party shall use such U.S. Commercialization Plan only to the extent necessary to carry out its Commercialization activities for the Product. From time to time as reasonably necessary during the term of Commercialization of a Product in the U.S., the JSC shall update the U.S. Commercialization Plan (it being understood that Affymax shall be responsible for generating draft updates relating to the Renal Indications and Takeda shall be responsible for generating draft updates relating to the Oncology Indications, for review and approval by the JSC).

**(b) For the Royalty Territory.** With respect to Level 1 Markets, the Level 2 Markets selected pursuant to Section 3.5(d) and such other countries in the Royalty Territory wherein Takeda Commercializes the Product, Takeda shall provide to the JSC a summary plan that describes the launch and subsequent Commercialization activities for the Product (including, if available, advertising, education, planning, marketing, sales force allocation, distribution, pricing, and reimbursement) (the "**ROW Commercialization Plan**"), to the extent customarily generated by or available to Takeda from its Affiliates or sublicensees for its internal purposes, and any significant amendments or updates thereto, without undue delay following creation thereof. The ROW Commercialization Plan shall be created by Takeda in good faith and in

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accordance with the overall strategy of Commercialization of the Product reviewed at the JSC. Each such plan shall include such additional information as Affymax may reasonably request and Takeda may reasonably accept from time to time.

### **5.3 Product Labeling; Promotional Materials.**

(a) The JSC shall determine which Party shall be responsible for designing and supplying the Product Labeling and Promotional Materials for the Product for the U.S. Such responsible Party shall provide samples of such labeling and materials to the JSC for review and consultation prior to finalizing such materials for use by the Parties' Sales Representatives. The Parties shall describe in the applicable Commercialization Plan how and the manner in which the Parties shall be presented and described to the medical community in any Promotional Materials and the placement of the names and logos of the Parties therein, in each case as permitted by applicable law and with the labeling for the Product approved by the applicable Regulatory Authority.

(b) Takeda shall be responsible for designing and supplying all Product Labeling and Promotional Materials for the Product for the Royalty Territory. Takeda shall provide samples of such labeling and materials to the JSC for information and review.

### **5.4 Pricing Approvals; Pricing.**

(a) U.S. Takeda shall have the sole right to determine all pricing of the Product in the U.S., subject to this Section 5.4(a) and Section 5.5. Takeda shall keep Affymax reasonably informed on an ongoing basis of current Product pricing for the U.S. by regular reports to the JSC no less frequently than such committee is required to meet pursuant to Section 2.5(a). Takeda shall provide Affymax with an opportunity, not to exceed [ \* ] (in case of initial price determination at the time of launch of each Product) or [ \* ] (in case of subsequent price modification(s)) following notice by Takeda, to review and comment upon Takeda's proposed price of the Product or any material modification thereof and shall consider Affymax's comments in good faith.

(b) **Royalty Territory.** Takeda shall be responsible, at its own expense, for seeking applicable Pricing Approval in the Royalty Territory and for setting the price of the Product in each applicable country. Takeda shall keep Affymax informed on an ongoing basis of current Product pricing in the countries of Royalty Territory wherein Takeda has launched the Product via regular reports to the JSC no less frequently than such committee is required to meet pursuant to Section 2.4(a). Notwithstanding anything in this Agreement express or implied to the contrary, Affymax shall not have any right to direct, control, or approve Takeda's pricing of the Product for the Royalty Territory. The provision to Affymax of any pricing data is for informational purposes only.

**5.5 Sales and Distribution.** Takeda shall be solely responsible for handling all returns, order processing, invoicing and collection, distribution, and inventory and receivables for the Product throughout the Licensed Territory. Affymax may not accept orders for the Product or make sales for its own account or for Takeda's account. If Affymax receives any order for the Product, it shall refer such orders to Takeda for acceptance or rejection. Takeda

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shall have the right and responsibility for establishing and modifying the terms and conditions with respect to the sale of the Product throughout the Licensed Territory, including any terms and conditions relating to or affecting the price at which the Product shall be sold, discounts available to any third party payers (including, without limitation, managed care providers, indemnity plans, unions, self insured entities, and government payer, insurance or contracting programs such as Medicare, Medicaid, or the U.S. Dept. of Veterans Affairs), any discount attributable to payments on receivables, distribution of the Product, and credits, price adjustments, or other discounts and allowances to be granted or refused; provided, however, that Takeda shall establish the terms and conditions applicable to the sale of the Product (including, without limitation, any discounts applicable to the Product) in a reasonable and non-discriminatory manner relative to other products sold by Takeda.

## **5.6 Takeda Performance; Diligence.**

(a) **Level of Efforts in the U.S. and Level 1 Markets.** Takeda shall devote Diligent Efforts to obtaining Regulatory Approval and thereafter Commercializing the Product in the U.S. and the Level 1 Markets. Without limiting the generality of the foregoing, Takeda shall devote Diligent Efforts to Commercialize the Product in the U.S. in the Field in accordance with the U.S. Commercialization Plan, and in the Level 1 Markets in accordance with the ROW Commercialization Plan.

(b) **Time to Launch Product.** In addition to the requirements under Section 5.6(a), Takeda shall achieve First Commercial Sale of each Product: (a) in [ \* ], within a reasonable time after, but in no event more than [ \* ] after, the date on which Pricing Approval is granted for such Product in such country, and (b) in any Level 1 Market other than those described in the preceding clause (a) (or in [ \* ], if Pricing Approval is not required in such country), within a reasonable time after, but in no event more than [ \* ] after, the date on which Regulatory Approval is granted for such Product in such country. If, however, it becomes difficult for Takeda to comply with the above-mentioned time limitations (i.e., [ \* ] in clause (a), and, [ \* ] in clause (b)), then Takeda shall without delay inform Affymax of the fact and explain the cause of such delay, and, such time limitations shall be extended to a reasonable extent if both Parties so agree.

(c) **Royalty Territory Reports.** Takeda shall present a written report to Affymax at least [ \* ] (and no later than [ \* ] of each Fiscal Year) summarizing Takeda's overall Commercialization activities undertaken with respect to the Product in or for the Royalty Territory pursuant to this Agreement, covering subject matter at a level of detail reasonably sufficient to enable Affymax to determine Takeda's compliance with its Diligent Efforts obligation pursuant to this Section 5.6.

**5.7 Co-Promotion in the U.S.** Affymax shall co-promote the Product in the Renal Indications in the U.S. jointly with Takeda pursuant to a co-promotion agreement describing the co-promotion activities of the Parties for the Product in such indications (the "**Co-Promotion Agreement**"). The Co-Promotion Agreement shall have the terms set forth in the term sheet attached to this Agreement as Exhibit L, as well as such other terms as the Parties may agree and as are customary in an agreement of that type. The Parties shall execute the Co-Promotion Agreement by such time as the JSC approves to be sufficiently prior to the then-current U.S.

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Approval Date in any Renal Indication. The “**Co-Promotion Term**” shall be set forth in the Co-Promotion Agreement and shall commence upon execution of the Co-Promotion Agreement and shall continue as long as the Co-Promotion Agreement remains effective. Unless terminated earlier in accordance with its terms, the Co-Promotion Agreement shall become effective as from the execution thereof and shall remain effective until the Generic Competition Date (as defined in Section 8.5(b)) in the U.S., and, thereafter, shall be extended automatically by periods of one (1) year unless either Party informs the other Party of its intention not to extend the Co-Promotion Agreement, with written notice to that effect given to the other Party no later than six (6) months prior to the then-current expiration date. If, in accordance with the previous sentence of this Section 5.7, a Party exercises its right not to extend the Co-Promotion Agreement, then the Co-Promotion Agreement shall expire on the then-current expiration date and this Agreement shall expire with regard to the U.S. in accordance with Sections 8.4 and 13.1 on the same date, provided, however, that, if in such case of expiration, if Affymax is the Party that exercised such right not to extend the Co-Promotion Agreement, then notwithstanding anything to the contrary contained in Article 13, Takeda shall be entitled to continue to use the Product Trademark in the U.S. for the Product on an exclusive basis (even as to Affymax) by paying Affymax a trademark royalty at the rate of [ \* ] of the Net Sales of the Product in the U.S.

#### **5.8 Sales Force Training for Commercialization in U.S.**

(a) All Affymax Sales Representatives shall be recruited by Affymax at Affymax's sole expense. All Takeda Sales Representatives shall be recruited by Takeda at Takeda's sole expense. For such recruitment, Takeda and Affymax shall jointly establish skill and experience criteria for Sales Representatives who will Detail the Product to target prescribers. At the request of Affymax, Takeda shall, to the extent Takeda deems reasonable, provide Affymax with Takeda's know-how and information which may be useful in the Affymax's recruitment of its Sales Representatives. Appropriate number of Affymax Sales Representatives and Takeda Sales Representatives shall be made available by each Party for training so that both Parties' Sales Representatives will be given the training simultaneously in accordance with the then-current U.S. Approval Date of the Product for Renal Indication.

(b) Each Party shall be responsible for the training of its Sales Representatives who will Detail the Product; provided, however, that Takeda shall allow, upon request of Affymax, and only for the period until the [ \* ] for an Oncology Indication or until the [ \* ], whichever is earlier, Affymax's Sales Representatives to participate in the training held by Takeda for its own Sales Representatives for the Renal Indication. The expenses incurred by either Party for the training of its own Sales Representatives, including but not limited to travel, lodging, meals during such training period, the costs of trainers providing such training, the training facility and training materials, but excluding salary and benefits given by each Party to its Sales Representatives, shall be included in the Commercial Expenses.

**5.9 Compliance.** Each Party shall comply with all applicable Laws relating to activities performed or to be performed by such Party (or its Affiliates, contractor(s) or sublicensee(s)) under or in relation to the Commercialization of the Product pursuant to this Agreement. Each Party represents, warrants and covenants to the other Party that, as of the Effective Date and during the Term, such Party and its Affiliates have adequate procedures in place: (i) to ensure their compliance with such Laws; (ii) to bring any noncompliance therewith

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by any of the foregoing entities to its attention; and (iii) to promptly remedy any such noncompliance

**5.10** [ \* ]. The Parties acknowledge that [ \* ] of Product [ \* ] in the [ \* ] could [ \* ] the Product [ \* ]. Accordingly, [ \* ]: (i) [ \* ] commercialize the Product [ \* ]; or (ii) except as set forth in the preceding clause (i), [ \* ] Affiliate or Third Party [ \* ] for the Product [ \* ], in each case without [ \* ] regarding Takeda's or [ \* ] the Product [ \* ]. [ \* ] [ \* ] shall be required, which [ \* ] only if [ \* ] that [ \* ] of the Product ([ \* ]) [ \* ] for that purpose. [ \* ] any and all such [ \* ], and to use Diligent Efforts to [ \* ] with [ \* ].

#### **5.11 Trademarks.**

**(a) Use.** Takeda shall use the Product Trademarks in connection with the Commercialization of the Product throughout the Licensed Territory; provided, that if the Product Trademarks in existence as of the Effective Date are not eligible for trademark protection in connection with the Product in one or more countries in the Licensed Territory, then the JSC shall identify alternative trademarks owned, registered or to be registered by Affymax and to be used for the Product in such countries only, for Takeda's final selection from among such trademarks identified by the JSC, and the Parties shall amend this Agreement to identify such marks and include them as Product Trademarks for the applicable countries. To the extent allowable by applicable Law in each country within the Licensed Territory, Product packaging, Promotional Materials and Product Labeling for use in the Licensed Territory shall carry, in a conspicuous location, the Affymax House Marks, subject to Takeda's reasonable approval of the size, position and location thereof.

**(b) Filing; Maintenance.** Affymax shall solely be responsible for and shall solely bear all costs of trademark searches, prosecution of applications to register and to record licenses (if applicable) for, and maintenance of, each Product Trademark and Affymax House Mark in the Licensed Territory; provided, however, that with respect to the U.S., such costs incurred by Affymax on or after the Effective Date shall be included in the Commercial Expenses. Affymax shall provide Takeda reasonable opportunity to review and comment on such prosecution efforts regarding the Product Trademarks in the Licensed Territory. Affymax shall provide Takeda with a copy of material communications from any trademark office in the Licensed Territory regarding such Product Trademarks, and shall provide Takeda with drafts of any material filings or responses to be made to such trademark office a reasonable amount of time in advance of submitting such filings or responses.

**(c) Ownership.** Affymax shall continue to own, throughout the world, any Product Trademarks and Affymax House Marks. All goodwill attributable to a Product Trademark or Affymax House Mark generated by the Commercialization of a Product bearing such marks shall inure to the benefit of Affymax.

**(d) Registration of Exclusive License.** Upon request of Takeda and as far as legally permissible, Affymax shall register before the relevant Governmental Authority that Takeda is the exclusive licensee under the Product Trademarks pursuant to this Agreement.

(e) **Compliance with Guidelines.** Takeda shall provide Affymax with exemplars or representative samples of primary (as reasonably agreed by the Parties) Promotional Materials and Product Labeling containing any Product Trademarks and Affymax House Mark which are intended to be broadly distributed or direct-to-consumer prior to using or disseminating such materials, if and to the extent such materials are used in the Royalty Territory and are substantially different from the form and presentation already approved by the JSC to be used in the U.S. Affymax shall have the right to make reasonable objections to any such materials within five (5) Business Days of Affymax's receipt of such exemplars or samples on the grounds that Affymax believes in good faith that the use of such materials will damage the reputation for quality associated with the Product Trademarks or Affymax House Marks. Takeda agrees to modify such Promotional Materials and Product Labeling in accordance with such objections of Affymax as far as it is reasonable. Takeda acknowledges Affymax's sole ownership of the Product Trademarks and Affymax House Marks and agrees not to take any action inconsistent with such ownership. Takeda covenants that it shall not use any trademark confusingly similar to any Product Trademarks or Affymax House Marks in connection with any products (including the Product). Takeda shall comply with reasonable policies provided by Affymax from time to time to maintain the goodwill and value of the Product Trademarks and Affymax House Marks, subject that such policies are not detrimental to the Commercialization of the Product and are in line with the relevant Laws. In any Takeda materials in which the Product Trademarks or Affymax House Marks appear, Takeda shall display a trademark legend in substantially the following form (tailored to reflect which trademark is being used): "[ \* ]<sup>TM</sup>" is a trademark owned by Affymax" Affymax grants no rights in the Product Trademarks or Affymax House Marks other than those expressly granted in Section 6.2.

## ARTICLE 6

### LICENSES AND PARALLEL PROGRAMS

**6.1 Licenses to Takeda under Affymax Technology.** Subject to the terms and conditions of this Agreement, Affymax hereby grants Takeda an exclusive (even as to Affymax, subject to the rights and obligations of Affymax under this Agreement), royalty-bearing (as provided in Article 8) license under the Affymax Technology to use and import Hematide in the Field in the Licensed Territory, to Develop (as and to the extent permitted in this Agreement), use, sell, offer for sale, and import the Bulk API and/or the Product in the Field in the Licensed Territory, and to make and have made the Finished Product anywhere in the world for such Development or sale (subject to Article 7) in the Field in the Licensed Territory. The license granted in this Section 6.1 may be sublicensed by Takeda to any Affiliate of Takeda without any need to obtain any further consent from Affymax, whether oral or in writing, subject to Section 5.10. Further, the license granted in this Section 6.1 may be sublicensed by Takeda to Third Parties only in the Royalty Territory and only with the prior written consent of Affymax, not to be unreasonably withheld and subject to Section 5.10. For clarity, the foregoing license does not permit Takeda to Develop using the Affymax Technology any Replacement Product Candidate, Backup Compound, Additional Product or any other derivative or analogue of the Peptide[ \* ] or Hematide, except to the extent it obtains such right pursuant to Sections 3.8, 3.9 and 3.12.

**6.2 Limited License for Product Trademarks and Affymax House Marks.** Affymax hereby grants to Takeda, during the Term, an exclusive, royalty-bearing license (as

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provided in Section 8.5) within the Licensed Territory to use and display the Product Trademarks and Affymax House Marks solely in the Promotional Materials and the Product Labeling in connection with the Commercialization of the Product within the Licensed Territory, as provided under and in accordance with Section 5.11 of this Agreement; provided that such license shall be co-exclusive with Affymax in the U.S. and further that Affymax may use such co-exclusive right solely for the Commercialization of the Product within the U.S. with Takeda hereunder. The foregoing license may be sublicensed by Takeda to its Affiliates and Third Parties sublicensees under the license granted in accordance with Section 6.1.

**6.3 License to Affymax under Takeda Technology.** Subject to the terms and conditions of this Agreement, Takeda hereby grants to Affymax a non-exclusive, royalty-free license under the Takeda Technology to develop, use, and promote the Product in the U.S., and to make and have made the Peptide, [ \* ] or Bulk API anywhere in the world for the Development or the Commercialization by the Parties in the Licensed Territory under this Agreement during the Term. Such license shall be sublicenseable by Affymax to any Affiliate of Affymax. Such license shall also be sublicenseable to any Third Party contract manufacturers of the Peptide, [ \* ] or Bulk API, only with the prior written consent of Takeda, such consent not to be unreasonably withheld.

**6.4 Negative Covenant.** Each Party covenants that it shall not use or practice any of the other Party's intellectual property rights licensed to it under this Article 6 except for the purposes expressly permitted in the applicable license grant under this Agreement.

**6.5 No Implied Licenses.** Except as explicitly set forth in this Agreement, neither Party grants any license, express or implied, under its intellectual property rights to the other Party.

#### **6.6 Parallel Programs.**

(a) If, during the Term, Takeda or its Affiliates, either on their own or in collaboration with a Third Party, market, promote or sell, directly or indirectly, in the Licensed Territory for the prevention, treatment or amelioration of [ \* ] any therapeutic agent, other than the Product, that includes or is comprised of an ESA, without Affymax's prior written consent (a "**Restricted Product**"), then Affymax may, as its sole remedy therefor, upon written notice to Takeda, in Affymax's sole discretion elect one of the following: (i) [ \* ] [ \* ] [ \* ], or (ii) [ \* ], [ \* ] [ \* ] [ \* ]. For avoidance of doubt, this Section 6.6 does not restrict Takeda's or its Affiliates' research and development activities with regard to ESAs, provided that Takeda acknowledges that it is not granted a license under the Affymax Technology to conduct such activities.

(b) Affymax, or its Affiliates, either on their own or in collaboration with a Third Party, hereby covenants and agrees, during the Term, not to market, promote or sell, directly or indirectly, in the Licensed Territory a product for the prevention, treatment or amelioration [ \* ] that includes or is comprised of an [ \* ], a Backup Compound or an ESA (other than the Product in accordance with this Agreement). For the avoidance of doubt, the foregoing covenant shall not in any way limit Affymax's ability (i) to perform research and development of ESAs for [ \* ], and (ii) to develop and commercialize [ \* ], Backup Compound or any other product in the field of [ \* ] or any indication other than the prevention, treatment or amelioration

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of [ \* ], provided that Affymax acknowledges that, except for the purpose of the Backup Research Agreement, it is not granted a license under the Takeda Technology to conduct such activities.

## **6.7 Third Party Licenses.**

(a) Takeda understands and acknowledges that certain rights contained within the Affymax Technology have been licensed to Affymax from certain Third Parties pursuant to those license agreements entered into as of the Effective Date and set forth in Exhibit I (the “**Existing Third Party License Agreements**”) and that Takeda’s rights under such Affymax Technology are subject to the following terms and conditions set forth in such agreements: (i) [ \* ] Nektar Agreement, which provides that [ \* ] (including without limitation [ \* ] granted to Takeda under this Agreement) shall [ \* ], and (ii) [ \* ] Nektar Agreement, which provides that the terms [ \* ] the terms and conditions [ \* ] Promptly after the Effective Date, Affymax shall use commercially reasonable efforts to request [ \* ] that, in the event that [ \* ] (other than [ \* ] this Agreement), Affymax shall be entitled to receive [ \* ] for [ \* ] contemplated hereunder, provided that in no event shall the failure [ \* ] commercially reasonable efforts [ \* ]. Affymax shall allow and fully cooperate with Takeda in connection with [ \* ]; if Affymax fails to [ \* ] within a reasonable time, then Takeda upon reasonable advance written notice to Affymax, may [ \* ]. The foregoing provision of this Section 6.7(a) shall apply *mutatis mutandis* to the situation where the [ \* ] is actually terminated for any reason and both Parties need a license under the [ \* ] for the purpose of this Agreement. Affymax shall, during the Term, maintain the Third Party License Agreements in full force and effect and shall not amend or modify such Third Party License Agreements in a manner that would reasonably be expected to have an adverse affect on Takeda’s rights and obligations hereunder and Takeda’s efforts to Develop and Commercialize the Product in the Field and in the Licensed Territory.

(b) In the event that a Party believes that a license under certain Third Party technology would be necessary or useful with respect to the Development and Commercialization of the Product in the Licensed Territory, then such Party shall notify the JSC. The Parties, working through the JSC, shall cooperate to obtain any such licenses under such terms and conditions as may be authorized by the JSC. Any acquisition or license agreement entered into by the Parties in accordance with this Section 6.7(b) shall be hereinafter called a “**Future Third Party License Agreement.**” The effects of payments made under Future Third Party License Agreements on royalties payable hereunder are described in Section 8.6(b).

**6.8 Amendment to Japan Agreement.** The Parties agree to use good faith and reasonable efforts to amend the Japan Agreement, within [ \* ] after the Effective Date, to reflect that Takeda is the licensee of Product both for the Licensed Territory and for Japan (including, without limitation, by deleting portions of the Japan Agreement that are no longer applicable).

## **ARTICLE 7**

### **MANUFACTURE AND SUPPLY**

**7.1 Roles of the Parties.** Affymax shall supply, or cause to be supplied through its Third Party contract manufacturers, in a timely manner, Takeda’s entire requirements of Bulk

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API for the Development and Commercialization of the Product by the Parties in or for the Licensed Territory, in accordance with this Article 7 and the Supply Agreement. Takeda shall be responsible for the formulation of Bulk API supplied to it by Affymax into the Finished Product and the manufacture of Finished Product (including stability testing) for the Development and Commercialization of the Product by the Parties in or for the Licensed Territory.

**7.2 Preclinical and Clinical Supply.** Affymax shall, by itself or through its Third Party contract manufacturers, supply to Takeda all quantities of Bulk API reasonably required by Takeda to Develop the Product in the Licensed Territory pursuant to the U.S. Development Plan and a plan for the ROW Development. Takeda shall, by itself or through its Third Party contract manufacturers and by using the Bulk API thus supplied by Affymax, supply to both Parties all quantities of Finished Product reasonably required to Develop the Product in the Licensed Territory pursuant to the U.S. Development Plan and a plan for the ROW Development. Such quantities of Bulk API and Finished Product, and the schedule for such supply, shall be confirmed and if necessary updated by the JSC in a manner consistent with the U.S. Development Plan and a plan for the ROW Development. Such supply shall be governed by clinical supply and Bulk API manufacturing agreements that the Parties shall negotiate in good faith promptly within ninety (90) days following the Effective Date. The clinical supply agreement shall, in addition to other terms and conditions agreed upon by the Parties, provide for the following:

(a) Affymax shall, before entering into negotiation for an agreement with a Third Party contract manufacturer of Bulk API for supply to Takeda hereunder, notify Takeda of the fact. Thereafter, Takeda shall have the right to provide input regarding the terms of such agreement (as well as any amendments thereof), review and comment on agreement drafts and forms, consult with Affymax regarding the negotiation of such agreement, and participate in person in the negotiation of such agreement, as the Parties may agree, it being understood that Affymax shall retain the final authority over the terms and conditions of any such agreement with such Third Party contractor. The Parties agree that [ \* ] should be qualified to manufacture Bulk API.

(b) From time to time, Takeda shall submit to Affymax purchase orders for quantities of Bulk API for such use consistent, as far as reasonably practicable, with such confirmed, or, if applicable, updated quantity and schedule which confirmation or update shall be consistent, as much as reasonably possible, with the then-current U.S. Development Plan and a plan for the ROW Development, and Affymax shall supply or have supplied to Takeda such quantities of Bulk API. All shipments to Takeda of Bulk API shall be made [ \* ].

(c) Affymax shall invoice Takeda for such Bulk API with each shipment, and Takeda shall pay such invoices within thirty (30) days of its receipt of such invoice. The price for supplies from Affymax to Takeda of Bulk API for (non-clinical and clinical) Development of the Product shall be [ \* ] for such Bulk API. The price of Bulk API used for the U.S. Development as well as the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Bulk API shall be included in the Development Expenses.

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(d) All Bulk API supplied by Affymax to Takeda shall, when delivered, have been manufactured, handled and stored by Affymax or its Third Party contract manufacturer(s) in compliance with all agreed-upon specifications and applicable Laws, including without limitation then-current GMP requirements.

(e) Subject to the following Section 7.2(f), the terms described in Sections 7.2(a), (b) and (d) above shall apply, *mutatis mutandis*, to Takeda's provision of Finished Product to Affymax, it being understood that Affymax shall provide Finished Product to both Parties during such time as Takeda is establishing a source of Finished Product, not to exceed [ \* ] after the Effective Date, unless mutually agreed upon otherwise by the Parties, and the terms described in Section 7.2(c) above shall apply, *mutatis mutandis*, to Affymax's provision of Finished Product to Takeda.

(f) With regard to the Finished Product manufactured by or on behalf of Takeda and provided to Affymax, Takeda shall not invoice Affymax. The Manufacturing Cost incurred by Takeda for the Finished Manufacture of the Finished Product thus provided to Affymax or used by Takeda for the U.S. Development, as well as the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Finished Product supplied to Affymax or used by Takeda, shall be included in the Development Expenses. Likewise, the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Affymax with regard to such Finished Product supplied to Affymax by Takeda, shall be included in the Development Expenses.

(g) Within [ \* ] after the Effective Date, the Parties shall discuss and agree upon the terms pursuant to which Affymax shall provide to Takeda reasonable quantities of: (i) reference standard compounds to the extent same are required to exercise methods in Product specifications; and (ii) related substances, both (i) and (ii) to the extent reasonably necessary for Takeda to Develop the Product. Provision of other non-Product synthetic peptides (*i.e.*, placebo) by Affymax to Takeda for Product development purposes shall be discussed by the JSC and Affymax shall supply these at [ \* ] cost of preparation to Takeda as soon as reasonably practicable after approval by the JSC.

For the purpose of this Section 7.2, both Parties shall abide by the above-mentioned (a) to (g) prior to the conclusion of a clinical supply agreement.

**7.3 Commercial Supply Agreement.** The Parties shall timely negotiate in good faith and enter into a manufacturing and supply agreement (the "**Supply Agreement**") governing the supply of Bulk API, by or on behalf of Affymax, to Takeda for the manufacture of Finished Product for the Commercialization of the Product by the Parties hereunder, to execute such Supply Agreement [ \* ] for the Product in the Licensed Territory, or [ \* ], whichever is earlier. Such Supply Agreement shall contain customary terms governing such manufacturing and supply relationships, and shall provide as follows:

(a) Bulk API meeting the agreed specification and manufactured in accordance with the applicable laws including then current GMP shall be supplied by or on behalf of Affymax to Takeda in a timely manner consistent with established and agreed

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manufacturing and delivery schedules at a cost equal to [ \* ] the manufacture of such Bulk API (which [ \* ], with such supply to be [ \* ]).

(b) Affymax shall establish [ \* ] commercial Bulk API manufacture in a timely manner to ensure that Affymax meets its obligation to supply quantities of Bulk API ordered by Takeda under the Supply Agreement. Upon the material and uncured breach by Affymax of its defined supply obligations as set forth in the Supply Agreement, Takeda shall have the right to obtain transfer and Affymax shall have the obligation to give transfer free of charge to Takeda, without undue delay, of any and all manufacturing technology necessary to enable it to manufacture or have manufactured Bulk API to meet its requirements. If such transfer occurs, Affymax would grant, without prejudice to any other remedies that are available to Takeda, to Takeda any additional licenses necessary to enable Takeda to exercise the foregoing manufacturing right without requiring Takeda to pay any additional consideration for such licenses.

(c) Takeda shall be responsible for the Finished Manufacture, testing (including stability testing) and final release of the Finished Product for Commercialization in the Licensed Territory. With regard to the Finished Product manufactured by or on behalf of Takeda and used or sold for Commercialization in the U.S., the Manufacturing Cost incurred by Takeda for the Finished Manufacture of the Finished Product thus used or sold in the U.S. hereunder, as well as the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Finished Product shall be included in the Cost of Goods Sold in the calculation of the U.S. Product Profit.

**7.4 Cost Audit.** Each Party shall use Diligent Efforts to minimize the Manufacturing Cost while assuring the quality and availability of Bulk API or Finished Product, as applicable, and shall consider in good faith all reasonable input from the other Party for such purpose. Each Party shall maintain complete and accurate records in sufficient detail to permit the other Party to confirm the accuracy of the calculation of Manufacturing Cost and resulting supply price payments due under this Agreement or the Supply Agreement. Upon reasonable prior notice, such records shall be available during regular business hours for a period of three (3) years from the creation of individual records for examination at the auditing Party's expense, and not more often than once each Fiscal Year, by an independent certified public accountant selected by the auditing Party and reasonably acceptable to the audited Party, for the sole purpose of verifying the accuracy of the calculation of the supply price pursuant to this Agreement. Any such accountant shall not disclose the audited Party's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of amount of supply price due by the auditing Party under this Agreement. Any amounts determined by such accountant to be overpaid, if any, shall be reimbursed to the auditing Party within [ \* ] from issuance of the accountant's report, plus interest (as set forth in Section 8.7) from the original due date. Any amounts determined to be underpaid shall be paid within [ \* ] from the accountant's report. The auditing Party shall bear the full cost of such audit unless such audit discloses an overpayment of the amount actually owed during the applicable Fiscal Year of more than [ \* ], in which case the audited Party shall bear the full cost of such audit.

**7.5 Facility Audits.** Each Party shall be permitted to conduct an inspection or audit of the other Party's facility or a facility of any Third Party contract manufacturer under contract

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with such other Party for the manufacture and supply of the Bulk API or Finished Product, as applicable, in or for the Licensed Territory. The audited Party shall allow the auditing Party to make such inspection or audit of any such the audited Party facility, and shall exercise its rights under any agreement between the audited Party and any such Third Party contract manufacturer to enable the auditing Party to make such inspection or audit of such Third Party contract manufacturer's facility, in each case to the extent relevant to the Bulk API or Finished Product supplied in or for the Licensed Territory and during normal business hours. The audited Party shall reasonably cooperate with the auditing Party to facilitate such inspection or audit. Any such inspection or audit by the auditing Party pursuant to this Section 7.5 shall be conducted no more frequently than once every year at a given facility, and shall occur as promptly as possible following written notice by the auditing Party of its desire for such inspection or audit, but in no event later than [ \* ] thereafter (unless such audit is triggered by a material safety issue, in which case the maximum notice period shall be [ \* ] ). Notwithstanding the foregoing, if any notice or observation is made by a Regulatory Authority of noncompliance of such facility with applicable Law in connection with Bulk API, the auditing Party may conduct an inspection or audit of such manufacturing facility more frequently than provided in the prior sentence to the extent necessary to confirm that the relevant matters in such notice or observation are adequately addressed. The Supply Agreement shall include additional rights of audit and inspection of facilities used to manufacture Bulk API to be supplied to Takeda in circumstances other than those described in this Section 7.5, to the extent and on such terms as the Parties may reasonably agree. Costs associated with auditing shall be solely borne by the auditing Party.

**7.6 Quality Agreement.** The Parties shall negotiate in good faith and enter into a quality agreement governing the quality control, quality assurance and validation of the commercial and clinical supply of the Bulk API to Takeda by or on behalf of Affymax and the commercial and clinical supply of Finished Product by or on behalf of Takeda. The Parties acknowledge and understand that, in order for the Product to be Commercialized in the Licensed Territory, Bulk API supplied to Takeda by Affymax hereunder must be manufactured, handled and stored in compliance with the GMP required by various Regulatory Authorities in the Licensed Territory. Accordingly, the quality agreement shall incorporate a provision stating that, should GMP as required by a particular Regulatory Authority impose additional or different obligations than are imposed under GMP as required by the FDA, then each Party shall, itself or through a Third Party contract manufacturer acting on behalf of that Party, comply with such GMP requirements with respect to Bulk API supplied to Takeda pursuant to this Agreement for use in the applicable country or territory; provided that (i) Takeda has previously notified Affymax in writing of such additional or different obligations, (ii) Affymax shall have a reasonable time after receiving such notice to comply with such additional or different obligations, and (iii) that Takeda shall cooperate to a reasonable extent with Affymax to enable Affymax to comply with such obligations.

**7.7 [ \* ] Source.** The Parties shall establish [ \* ] of Bulk API manufacturing and [ \* ] of Finished Manufacture as follows: (i) Affymax shall be responsible for screening potential manufacturers, negotiating the applicable supply agreement, and effecting the technology transfer as necessary to establish and qualify [ \* ] Bulk API manufacturers, whether those are Affymax, its Affiliates, or Third Parties; provided, that, Takeda shall have the right to provide input regarding the terms of such agreements (as well as any amendments thereof), review and

comment on agreement drafts and forms, consult with Affymax regarding the negotiation of such agreements between Affymax and Third Party contract manufacturers, and [ \* ], as the Parties may agree, it being understood that Affymax shall retain the final authority over the terms and conditions of any such agreements with such Third Party contractors; (ii) Takeda shall be responsible for screening potential Finished Product manufacturers, negotiating the applicable supply agreements, and effecting the technology transfer as necessary to establish and qualify [ \* ] Finished Product manufacturers, whether those are Takeda, its Affiliates or Third Parties; and (iii) in any event, Affymax shall have the right, upon written notice to Takeda and at Affymax's cost, to establish additional sources of Finished Manufacture, other than Takeda or its Affiliates, at Affymax's cost and discretion. In case the manufacturing sources are not the Parties or their Affiliates but rather are Third Party contractors, then the costs incurred by the Parties in connection with the establishment of such manufacturing sources pursuant to the above subsection (i) or (ii), shall be treated as Commercial Expenses.

## ARTICLE 8

### COMPENSATION

**8.1 License Fee.** No later than [ \* ] Business Days after the Effective Date, Takeda shall pay to Affymax a license fee of One Hundred Five Million Dollars (\$105,000,000) by wire transfer of immediately available funds into an account designated by Affymax in writing; provided, that if Affymax has not provided Takeda with two copies, properly completed by and with original signatures of Affymax, of document(s) necessary to claim the benefit of an income tax treaty (i.e., Form 3, "Application Form for Income Tax Convention", because Takeda already has Form 17, "Attachment Form For Limitation On Benefits Article" which was given by Affymax under the Japan Agreement), for submission to the Japanese tax authorities on or before the Effective Date, then such due date shall be extended to be no later than [ \* ] Business Days after the day such form is received by Takeda. Such license fee shall be non-refundable and non-creditable against any other payments due hereunder.

**8.2 Development Milestone Payments.** Takeda shall make milestone payments to Affymax based on the first achievement of each milestone event in the Licensed Territory for the Product as set forth in this Section 8.2. Takeda shall pay to Affymax the amounts set forth below within [ \* ] after the first achievement of the corresponding milestone event with respect to the Product. Each such payment shall be made by wire transfer of immediately available funds into an account designated by Affymax. Each milestone payment by Takeda to Affymax hereunder shall be payable only once, regardless of the number of times achieved by one or more Products. Each such payment is non-refundable and non-creditable against any other payments due hereunder.

<i>Milestone Event</i>	<i>Milestone Payment</i>
[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]

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[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]
<b>Total Milestone Payments</b>	\$280,000,000
<sup>(1)</sup> For clarity, [ * ] <sup>(2)</sup> For purposes of this section, “completion” means [ * ] <sup>(3)</sup> For clarity, the [ * ] milestone for [ * ] shall be payable upon the [ * ] <sup>(4)</sup> For clarity, the milestones for [ * ] shall be payable upon [ * ] <sup>(5)</sup> For clarity, if [ * ] milestones will be payable [ * ]	

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**8.3 Sales Milestone Payments.** Takeda shall make milestone payments to Affymax based on the first achievement of each milestone event in the Licensed Territory as set forth in this Section 8.3. Takeda shall pay to Affymax the amounts set forth below as soon as reasonably possible after Takeda recognizes and confirms the first achievement of the corresponding milestone event with respect to the Product but in no event later than within [ \* ] after the end of a calendar quarter in which the corresponding milestone event is achieved; provided, however, that if Affymax reasonably believes that a milestone has been achieved, then Affymax shall notify the Finance Subcommittee, which shall promptly assess the situation and send a recommendation to the JSC and the JSC shall determine whether such milestone has been met. If the JSC confirms that such milestone has been met, then Takeda shall make the corresponding milestone payment within [ \* ] Business Days from such confirmation. Each such payment shall be made by wire transfer of immediately available funds into an account designated by Affymax in writing. Each milestone payment by Takeda to Affymax hereunder shall be payable only once, regardless of the number of times achieved by one or more Products. Each such payment is non-refundable and non-creditable against any other payments due hereunder.

<i>Milestone Event</i>	<i>Milestone Payment</i>
[ * ]	
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]
[ * ]	[ * ]

**8.4 Sharing of U.S. Expenses and U.S. Product Profit.** During the Co-Promotion Term, Affymax and Takeda shall share equally in the U.S. Product Profit for each Finished Product. Within [ \* ] of the end of each calendar quarter following the First Commercial Sale of the Finished Product in the U.S., each Party shall report to the Finance Subcommittee its revenues and individual Commercial Expense items (with appropriate supporting information) involved in the computation of U.S. Product Profit and accrued during such quarter with respect to each such Finished Product. Such reports shall be in such form as the Parties may agree from time to time. The JSC and the Finance Subcommittee shall create and maintain procedures for the reporting and implementation of Profit Equalization Payments with respect to each Collaboration Product. In addition, Takeda shall provide Affymax with a monthly statement of the amount of gross sales of Product in the U.S. Notwithstanding the foregoing, with regard to the Commercial Expenses incurred by either Party before the First Commercial Sale in the U.S., the Parties shall calculate and equally share them on a calendar quarterly basis and shall make

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reconciliation, if necessary for this purpose of equal sharing, within [ \* ] after each calendar quarter.

## 8.5 Royalties.

(a) **Royalty Rate.** Takeda shall pay to Affymax royalties based on the aggregate annual Net Sales of the Finished Product sold in the Royalty Territory at the rates set forth below:

(i) [ \* ] aggregate Net Sales of such Product in the Royalty Territory during a Fiscal Year that is equal to or less than [ \* ];

(ii) [ \* ] aggregate Net Sales of such Product in the Royalty Territory during a Fiscal Year that is greater than [ \* ] but equal to or less than [ \* ]; and

(iii) [ \* ] aggregate Net Sales of such Product in the Royalty Territory during a Fiscal Year that exceeds [ \* ].

For the purpose of calculation of “the aggregate annual Net Sales of the Finished Product sold in the Royalty Territory” mentioned above, the Net Sales of the Product sold in a country of the Royalty Territory on and after the Generic Competition Date (as defined in Section 8.5(b)) in such country shall be excluded.

(b) **Royalty Rate Step Down.** Takeda acknowledges that it shall continue to enjoy substantial benefit from its license under, and the transfer to Takeda of certain elements of, the Affymax Technology pursuant to this Agreement (including without limitation the Affymax Know-How licensed to Takeda, and the regulatory data to be provided to Takeda, pursuant to this Agreement) as well as from Takeda’s own development of Takeda Technology derived from the practice of such license and Takeda’s use of such Affymax Technology, even after expiration of all Valid Claims of the Affymax Patents and Joint Patents covering the composition of matter of the Product in a country in the Licensed Territory, determined on a country-by-country basis (and Product-by-Product basis if applicable) (the date upon which the last to expire of such Valid Claims occurs for the Product in a particular country, the “**Expiration Date**”). Accordingly, Takeda shall, on a country-by-country (and Product-by-Product basis if applicable), continue to pay royalties on Net Sales of Product by Takeda, its Affiliates and sublicensees after the Expiration Date in the applicable country, in consideration for the foregoing non-patent benefits, at rates equal to [ \* ] of the rates set forth in Section 8.5(a) above (resulting in royalty rates of [ \* ], which shall also apply to the royalties to be paid from First Commercial Sale for the Net Sales in countries of the Royalty Territory wherein there is no Affymax Patents covering the composition of matter of the Product). Such reduced royalty rates shall continue in effect, on a Product-by-Product and country-by-country basis, until the end of the second consecutive quarterly period during which one or more Third Parties have [ \* ] of such Product in such country equal to or greater than [ \* ] such Product [ \* ] taken together in the aggregate (such date, the [ \* ]). After the [ \* ], Takeda shall continue to pay royalties equal to [ \* ] of Net Sales of Product by Takeda, its Affiliates and sublicensees in the applicable country of the Royalty Territory, in consideration for the use of the Product Trademark. Such royalty of [ \* ] shall be payable for so long as Takeda is selling the Product in such country using the Product

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Trademark. As used in this Section 8.5(b), “[ \* ]” means [ \* ] Product and that has [ \* ] through [ \* ] under [ \* ] the foregoing that [ \* ] the Product.

(c) **Royalty Payments and Reports.** All amounts payable to Affymax pursuant to this Section 8.5 shall be paid in Dollars on a calendar quarter basis, subject to semi-annual reconciliation, in accordance with this Section 8.5(c). Takeda shall, within [ \* ] of the end of each calendar quarter, deliver Affymax a non-binding estimate of the amounts payable to Affymax pursuant to this Section 8.5 based on the estimated Net Sales of the Product in the Royalty Territory during such calendar quarter (the “**Estimated Royalty**”) and shall provisionally pay to Affymax the Estimated Royalty for the calendar quarter. It is understood that the exact amount of the Net Sales in the Royalty Territory for such calendar quarter as well as the IMS or other data necessary to determine whether the [ \* ] has come or not in a certain country or countries of the Royalty Territory may not be available for the purpose of calculation of the Estimated Royalty, and Takeda may calculate the Estimated Royalty from the flash report then available to Takeda (for gross sales) and deduction therefrom at the rate of [ \* ] during the first [ \* ] following the First Commercial Sale in the Royalty Territory; and, within a reasonable time after such [ \* ] period, the appropriateness of the rate of such deductions shall be reviewed by the Parties based on the actual deductions for the Product since the First Commercial Sale thereof and, the rate of deduction applied thereafter, upon mutual agreement between the Parties, shall be modified or adjusted based on such actual deductions, and, if necessary, be further reviewed, modified or adjusted from time to time upon mutual agreement. Takeda shall, within [ \* ] after the end of each half of the Fiscal Year, deliver Affymax a fixed report of the amount which should have actually been paid to Affymax, pursuant to this Section 8.5, for the Net Sales in such half of the Fiscal Year as well as the report with respect to the amount to be paid from one Party to the other Party for reconciliation of the difference between the Estimated Royalties paid by Takeda to Affymax and the actual amount to have been paid by Takeda to Affymax, pursuant to this Section 8.5, for the actual Net Sales during the same half of the Fiscal Year. Within [ \* ] after Affymax’s receipt of such reports, both Parties shall make reconciliation accordingly (i.e., by Affymax’s paying the amount owed to Takeda (in the case of excess payment by Takeda) or by Takeda’s paying the amount owed to Affymax (in the case of short payment by Takeda)) for the same half Fiscal Year, without one Party being required to pay the other Party any interest thereon. Takeda shall provide Affymax with a monthly flash statement of the amount of gross sales of Product in the Royalty Territory during the applicable month. Each fixed report delivered by Takeda to Affymax once every half of the Fiscal Year mentioned above shall include a monthly statement of the amount of gross sales of Product in the Royalty Territory during the applicable half of the Fiscal Year, an amount of Net Sales in the Royalty Territory during such half of the Fiscal Year with quarterly breakdown, and a calculation of the amount of royalty payment due on such sales for such half of the Fiscal Year with quarterly breakdown. Takeda shall require its sublicensees to account for their Net Sales and to provide such reports with respect thereto so that Takeda can fulfill the above-mentioned obligation in this Section 8.5(c).

## **8.6 Third Party Payments.**

(a) **Existing Agreements.** In addition to the royalties owed pursuant to Section 8.5, Takeda shall reimburse Affymax for those royalties set forth on Exhibit I due to Third Parties pursuant to the Existing Third Party License Agreements (as listed on Exhibit I)

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with respect to the Commercialization of the Product in the Royalty Territory by Takeda, its Affiliates or sublicensees. All royalties set forth on Exhibit I due to Third Parties pursuant to the Existing Third Party License Agreements with respect to the Commercialization of the Product in the U.S. shall be included in the Commercial Expenses.

**(b) Future Agreements.** Except as provided in Section 9.13, both Parties, through their involvement in the JSC, shall participate in the negotiation of Future Third Party License Agreements pursuant to Section 6.7(b). The royalties, milestones, and other payments due to Third Parties in respect of the license or acquisition of any Third Party technology pursuant to a Future Third Party License Agreement, if concluded by Affymax and/or Takeda with a Third Party with respect to the Development and Commercialization of the Product in the Royalty Territory under this Agreement shall be borne by Takeda; provided, that Takeda shall have the right to deduct up to [ \* ] of any such royalties, milestones, and other payments borne by Takeda from the amounts otherwise due to Affymax under Section 8.5 of this Agreement; provided, that in no event shall such deduction reduce the effective royalty rate payable to Affymax [ \* ]. By way of example, [ \* ] in [ \* ] [ \* ] in [ \* ]; (i) if the [ \* ] Affymax [ \* ] at that time is [ \* ] then there shall be [ \* ] and Takeda shall [ \* ] for [ \* ]; and, (ii) if the [ \* ] Affymax [ \* ] at that time is [ \* ], then Takeda shall [ \* ] such [ \* ] and [ \* ]. All royalties, milestones, and other payments due to Third Parties pursuant to the Future Third Party License Agreements with respect to the Development and Commercialization of the Product in the U.S. shall be included in the Commercial Expenses.

**(c) Reimbursement Procedures.** In the event that a Future Third Party License Agreement provides for payments that are not directly associated with the Development and/or Commercialization of the Product in a particular geographic territory, then such payments shall be allocated as follows for purposes of this Section 8.6: seventy percent (70%) to the U.S. and thirty percent (30%) to the Royalty Territory. On a quarterly basis, Affymax shall invoice Takeda for payments which Affymax actually made during such quarter to Third Parties to whom such payments are due under a Future Third Party License Agreement, and Takeda shall pay to Affymax such invoiced amount within thirty (30) days.

## **8.7 Taxes.**

**(a) Cooperation and Coordination.** The Parties acknowledge and agree that it is their mutual objective and intent to minimize, to the extent feasible and legal, taxes payable with respect to their collaborative efforts under this Agreement and that they shall use all commercially reasonable efforts to cooperate and coordinate with each other to achieve such objective.

**(b) Payment of Tax.** A Party receiving a payment pursuant to this Article 8 shall pay any and all taxes levied on such payment. If applicable Law requires that taxes be deducted and withheld from a payment made pursuant to this Article 8, the remitting Party shall promptly notify the other Party and provide all relevant information available to it and (i) deduct those taxes from the payment; (ii) pay the taxes to the proper taxing authority; and (iii) send evidence of the obligation together with proof of payment to the other Party within [ \* ] following that payment.

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(c) **Tax Residence Certificate.** A Party (including any entity to which this Agreement may be assigned, as permitted under Section 15.5) receiving a payment pursuant to this Article 8 shall provide the remitting Party appropriate certification from relevant revenue authorities that such Party is a tax resident of that jurisdiction (a “**Tax Residence Certificate**”), if such receiving Party wishes to claim the benefits of an income tax treaty to which that jurisdiction is a party. Upon the receipt thereof, any deduction and withholding of taxes shall be made at the appropriate treaty tax rate.

(d) **Assessment.** Either Party may, at its own expense, protest any assessment, proposed assessment, or other claim by any Governmental Authority for any additional amount of taxes, interest or penalties or seek a refund of such amounts paid if permitted to do so by applicable Law. The Parties shall cooperate with each other in any protest by providing records and such additional information as may reasonably be necessary for a Party to pursue such protest.

**8.8 Blocked Currency.** In each country where the local currency is blocked and cannot be removed from the country, royalties accrued in that country shall be paid to Affymax in Dollars and Takeda shall retain any amounts received in such restricted local currency, unless the Parties otherwise agree.

**8.9 Foreign Exchange.** The rate of exchange to be used in computing the amount of currency equivalent in Dollars owed to a Party under this Agreement shall be made at the period-end rate of exchange quoted on the last day of the applicable calendar quarter by Citibank in New York City.

**8.10 Late Payments.** If a Party does not receive payment of any sum due to it on or before the due date, simple interest shall thereafter accrue on the sum due to such Party until the date of payment at the per annum rate of [ \* ] over the then-current prime rate quoted by Citibank in New York City, or the maximum rate allowable by applicable Law, whichever is lower.

**8.11 Records; Audits.** Each Party shall maintain complete and accurate records in sufficient detail to permit the other Party to confirm the accuracy of the calculation of payments to the other Party under this Agreement. Upon reasonable prior notice, such records shall be available during regular business hours of audited Party for a period of [ \* ] from the creation of individual records for examination at auditing Party’s expense, and not more often than once each Fiscal Year, by an independent certified public accountant selected by auditing Party and reasonably acceptable to audited Party, for the sole purpose of verifying the accuracy of the financial reports furnished pursuant to this Agreement. Any such auditor shall not disclose audited Party’s Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by audited Party or the amount of payments due by audited Party under this Agreement. Any amounts shown to be owed but unpaid shall be paid within [ \* ] from the accountant’s report, plus interest (as set forth in Section 8.6) from the original due date. Any amounts determined to be overpaid shall be refunded within [ \* ] from the accountant’s report. The auditing Party shall bear the full cost of such audit unless such audit discloses an underpayment of the amount actually owed during the applicable Fiscal Year of more than [ \* ], in which case audited Party shall bear the full cost of such audit.

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## ARTICLE 9

### INTELLECTUAL PROPERTY MATTERS

**9.1 Ownership of Inventions.** Each Party shall own any inventions made solely by its employees, agents, or independent contractors in the course of conducting its activities under this Agreement, together with all intellectual property rights therein ("**Sole Inventions**"). Any inventions that are made jointly by employees, agents, or independent contractors of each Party in the course of performing activities under this Agreement, together with all intellectual property rights therein ("**Joint Inventions**") shall be owned jointly by the Parties in accordance with joint ownership interests of co-inventors under U.S. patent Laws, with each Party having, unless otherwise set forth in this Agreement, the unrestricted right to license and grant rights to sublicense each such Joint Invention, and each Party hereby agrees to consent, without payment of any further consideration or royalty, to the joint Party's licensing of said joint Party's interest in such Joint Invention to Third Parties. Inventorship shall be determined in accordance with U.S. patent Laws. Sole Inventions owned by Takeda and Takeda's interest in all Joint Inventions shall be included in the Takeda Technology. Sole Inventions owned by Affymax and Affymax's interest in all Joint Inventions shall be included in the Affymax Technology.

**9.2 Disclosure of Inventions.** Each Party shall promptly disclose to the other any invention disclosures, or other similar documents, submitted to it by its employees, agents or independent contractors describing inventions that may be either Sole Inventions or Joint Inventions, and all Information relating to such inventions.

### **9.3 Prosecution of Patents.**

**(a) Affymax Patents Other than Joint Patents.** Except as otherwise provided in this Section 9.3(a), Affymax shall have the sole right, authority and obligation to file, prosecute and maintain the Affymax Patents (other than Joint Patents which shall be prosecuted and maintained in accordance with Section 9.3(c)) on a worldwide basis. Affymax shall provide Takeda reasonable opportunity to review and comment on such prosecution efforts regarding such Affymax Patents in the Licensed Territory. Affymax shall provide Takeda with a copy of material communications from any patent authority in the Licensed Territory regarding such Affymax Patents, and shall provide Takeda with drafts of any material filings or responses to be made to such patent authorities a reasonable amount of time in advance of submitting such filings or responses. Notwithstanding the foregoing, if Affymax desires to abandon or not maintain any Patent within such Affymax Patents in the Licensed Territory, then Affymax shall provide Takeda with thirty (30) days prior written notice of such desire (or such longer period of time as reasonably necessary to allow Takeda to assume such responsibilities) and, if Takeda so requests, shall provide Takeda with the opportunity to prosecute and maintain such Patent in the Licensed Territory in place of Affymax, at Takeda's sole expense, in which case Affymax shall assign such Patent in the Licensed Territory to Takeda (and such Patent shall thereafter be included in the Takeda Patents). If Takeda desires Affymax to file, in the Licensed Territory, a patent application that claims priority from a Patent within the Affymax Patents, other than a Joint Patent, in the Licensed Territory, Takeda shall provide written notice to Affymax requesting that Affymax file such patent application in the Licensed Territory. If Takeda provides such written notice to Affymax, Affymax shall either (i) file and prosecute such patent

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application and maintain any patent issuing thereon in the Licensed Territory, at Affymax's expense, or (ii) notify Takeda that Affymax does not desire to file such patent application and provide Takeda with the opportunity to file and prosecute such patent application and maintain any patent issuing thereon in the Licensed Territory in place of Affymax, at Takeda's sole expense, in which case Affymax shall assign such patent application or a right to file such patent application described in (ii) to Takeda in the Licensed Territory (and in which case such Patent thus assigned to or filed by Takeda shall be included in the Takeda Patents).

(b) **Takeda Patents Other Than Joint Patents.** Except as otherwise provided in this Section 9.3(b), Takeda shall have the sole right and authority, but not an obligation, to prosecute and maintain the Takeda Patents other than Joint Patents on a worldwide basis at its sole discretion (subject to this Section 9.3(b)) and at its own cost and responsibility. Takeda shall provide Affymax reasonable opportunity to review and comment on such prosecution efforts regarding such Takeda Patents. Takeda shall provide Affymax with a copy of material communications from any patent authority regarding such Takeda Patents, and shall provide Affymax with drafts of any material filings or responses to be made to such patent authorities a reasonable amount of time in advance of submitting such filings or responses. If Takeda determines in its sole discretion to abandon or not maintain any Patent within the Takeda Patents other than a Joint Patent anywhere in the world, then Takeda shall provide Affymax with thirty (30) days' prior written notice of such determination (or such longer period of time reasonably necessary to allow Affymax to assume such responsibilities) and shall provide Affymax with the opportunity to prosecute and maintain such Patent in the applicable jurisdiction in place of Takeda at Affymax's sole expense, and if Affymax so requests, Takeda shall assign such Patent to Affymax (in which case such Patent shall be included in the Affymax Patents). If Affymax desires Takeda to file, in a particular jurisdiction, a patent application that claims priority from a Patent within the Takeda Patents, Affymax shall provide written notice to Takeda requesting that Takeda file such patent application in such jurisdiction. If Affymax provides such written notice to Takeda, Takeda shall either (i) file and prosecute such patent application and maintain any patent issuing thereon in such jurisdiction at Takeda's expense, or (ii) notify Affymax that Takeda does not desire to file such patent application and provide Affymax with the opportunity to file and prosecute such patent application and maintain any patent issuing thereon at Affymax's sole expense in place of Takeda, in which case Takeda shall assign such patent application or a right to file such patent application described in (ii) to Affymax (and in which case such Patent shall be included in the Affymax Patents).

(c) **Joint Patents.** With respect to any potentially patentable Joint Invention, the Parties shall meet and agree upon which Party shall prosecute and maintain patent applications covering such Joint Invention (any such patent application and any patents issuing therefrom a "**Joint Patent**") in particular countries and jurisdictions throughout the world. It is the intention of the Parties that, unless otherwise agreed, Takeda would prosecute and maintain any Joint Patents in the Licensed Territory other than the U.S., and Affymax would prosecute and maintain the Joint Patents in the U.S., subject to the Parties coordinating their efforts as appropriate to make such prosecution activities as efficient, convenient and harmonious as possible. The external costs of such prosecution of the Joint Patents shall be shared equally by the Parties and the internal costs of such prosecution of the Joint Patents shall be borne by the Party that prosecutes a patent application in the Joint Patents (the "**Prosecuting Party**"). The

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Prosecuting Party shall provide the other Party reasonable opportunity to review and comment on such prosecution efforts regarding the applicable Joint Patents in the particular jurisdictions, and such other Party shall provide the Prosecuting Party reasonable assistance in such efforts. The Prosecuting Party shall provide the other Party with a copy of all material communications from any patent authority in the applicable jurisdictions regarding the Joint Patent being prosecuted by such Party, and shall provide the other Party with drafts of any material filings or responses to be made to such patent authorities a reasonable amount of time in advance of submitting such filings or responses. In particular, each Party agrees to provide the other Party with all information necessary or desirable to enable the other Party to comply with the duty of candor/duty of disclosure requirements of any patent authority. Except to the extent a particular Party is restricted by the licenses granted to the other Party or the other covenants contained in and subject to the terms of the Agreement, each Party shall be entitled to practice, and grant to Third Parties and its Affiliates the right to practice, the Joint Patents and all Joint Inventions without restriction or an obligation to account to the other Party, and the other Party hereby consents, without additional consideration, to any and all such licenses. Either Party may determine that it is no longer interested in supporting the continued prosecution or maintenance of a particular Joint Patent in a country or jurisdiction, in which case: (i) such Party may elect to cease its ownership interest in such Joint Patents and shall, if requested in writing by the other Party, assign its ownership interest in such Joint Patent in such country or jurisdiction to the other Party for no additional consideration, and (ii) thereafter, the electing Party shall be released from any obligations with regard to such Joint Patents and any such Joint Patent would thereafter be deemed a Affymax Patent in the case of assignment to Affymax, or a Takeda Patent in the case of assignment to Takeda.

**(d) Cooperation in Prosecution.** Each Party shall provide the other Party all reasonable assistance and cooperation in the Patent prosecution efforts provided above in this Section 9.3, including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution.

**9.4 Patent Term Extensions in the Licensed Territory.** The internal patent counsel of each Party shall discuss and recommend for which, if any, of the Affymax Patents, Takeda Patents and Joint Patents in the Licensed Territory the Parties should seek Patent Term Extensions in the Licensed Territory, and, Affymax, in the case of the Affymax Patents, and Takeda in the case of the Takeda Patents and Joint Patents, shall have the final decision-making authority with respect to applying for any such Patent Term Extensions in the Licensed Territory, and shall act with reasonable promptness in light of the development stage of the Product to apply for any such Patent Term Extensions, where it so elects, *provided, however*, that if in the Licensed Territory only one such Patent can obtain a Patent Term Extension, then the Parties shall consult in good faith to determine which such Patent should be the subject of efforts to obtain a Patent Term Extension, and (a) in case of disagreement with respect to the U.S., the JSC shall determine which single Patent should be extended and (b) in case of disagreement with respect to the Royalty Territory, Takeda's decision on which single Patent to be extended shall control. The Party that does not apply for an extension hereunder shall cooperate fully with the other Party in making such filings or actions, for example and without limitation, making available all required regulatory data and information and executing any required authorizations to apply for such Patent Term Extension. All activities of the Parties pursuant to this Section 9.4

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for the Licensed Territory shall be at the expense of the Party who owns such extended Patents (in case of Joint Patents, expenses shall be shared equally by the Parties).

#### **9.5 Infringement of Patents by Third Parties.**

(a) **Notification.** Each Party shall promptly notify the other Party in writing of any existing or threatened infringement of the Affymax Patents, Joint Patents or Takeda Patents of which it becomes aware, and shall provide evidence in such Party's possession demonstrating such infringement.

##### **(b) Infringement of Affymax or Joint Patents in the Licensed Territory.**

(i) If a Party becomes aware that a Third Party infringes any Affymax Patent or Joint Patent in the Licensed Territory by making, using, importing, offering for sale or selling the Product, Hematide, [ \* ] or any product containing the Peptide, [ \* ] (such activities, "**Product Infringement**"), then such Party shall so notify the other Party as provided in Section 9.5(a), which such notice shall include all Information available to the notifying Party regarding such alleged infringement. The process for bringing a suit or action shall be as follows:

(1) In the U.S., Affymax shall have the first right, but not the obligation, to bring an appropriate suit or other action against any person or entity engaged in such Product Infringement, subject to Section 9.5(b)(ii) below, with such external expenses shared equally by the Parties (except as otherwise expressly provided in this Section 9.5(b)(i)(1)). Affymax shall have a period of [ \* ] after notification by a Party hereunder (or shorter period, if required by the nature of the possible proceeding), to elect to so enforce such Patent. In the event it does not so elect, it shall so notify Takeda in writing during such [ \* ] time period (or above-mentioned shorter period), and Takeda shall have the right, but not the obligation, to commence a suit or take action to enforce the applicable Patent against such Third Party perpetrating such Product Infringement, with such external expenses shared equally by the Parties (except as otherwise expressly provided in this Section 9.5(b)(i)(1)). Each Party shall provide to the Party enforcing any such rights under this Section 9.5(b)(i)(1) reasonable assistance in such enforcement, at such enforcing Party's request, including joining such action as a party plaintiff if required by applicable Law to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider the other Party's comments on any such efforts. Each Party shall bear all of its own internal costs incurred in connection with its activities under this Section 9.5(b)(i)(1). Any recoveries under this Section 9.5(b)(i)(1) shall first be applied to the recovery of external expenses incurred by both Parties in bringing the suit or action; and the remaining amounts, if any, shall be [ \* ].

(2) In the Royalty Territory, Takeda shall have the first right, but not the obligation, to bring an appropriate suit or other action against any person or entity engaged in such Product Infringement, subject to Section 9.5(b)(ii) below, at its sole cost and expense (except as otherwise expressly provided in this Section 9.5(b)(i)(2)). Takeda shall have a period of [ \* ] (or shorter period, if required by the nature of possible proceeding) after notification by a Party hereunder, to elect to so enforce such Patent. In the event Takeda does not so elect, it shall so notify Affymax in writing during such [ \* ] time period (or above-

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mentioned shorter period), and Affymax shall have the right, but not the obligation, to commence a suit or take action to enforce the applicable Patent against such Third Party perpetrating such Product Infringement at its sole cost and expense (except as otherwise expressly provided in this Section 9.5(b)(i)(2)). Each Party shall provide to the Party enforcing any such rights under this Section 9.5(b)(i)(2) reasonable assistance in such enforcement, at such enforcing Party's request, including joining such action as a party plaintiff if required by applicable Law to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider the other Party's comments on any such efforts. Any recoveries obtained from a suit or an action commenced by Takeda hereunder shall first be applied to the recovery of expenses incurred by Takeda in bringing the suit or action; and the remaining amounts, if any, shall be [ \* ]. Any recoveries obtained from a suit or an action commenced by Affymax shall be [ \* ].

(3) Notwithstanding anything to the contrary in this Section 9.5, Takeda acknowledges and agrees that, pursuant to Section 2.3(e) of the Nektar Agreement, neither Affymax nor Takeda shall have any enforcement rights with respect to the Enzon Patents.

(ii) The Party notified but not bringing an action with respect to Product Infringement in the Licensed Territory under Section 9.5(b) shall be entitled to separate representation in such matter by counsel of its own choice and at its own expense, but such Party shall at all times cooperate fully with the Party bringing such action. Additionally, the Party not bringing an action under this Section 9.5(b) may have an opportunity to participate in such action to the extent that the Parties may mutually agree at the time the other Party elects to bring an action hereunder.

(c) **Infringement of Takeda Patents (Other than Joint Patents) in the Licensed Territory.** For all infringement of any Takeda Patents (other than Joint Patents) in the Licensed Territory, Takeda shall have the exclusive right, but not the obligation, to bring, at Takeda's expense and in its sole control, an appropriate suit or other action against any person or entity engaged in such infringement of such Takeda Patent. Takeda shall have a period of [ \* ] (or shorter period, if required by the nature of possible proceeding) after notification by a Party under Section 9.5(a), to elect to so enforce such Patent. In the event Takeda does not elect to bring a suit or action, it shall so notify Affymax in writing during such [ \* ] time period (or above-mentioned shorter period), then Affymax shall have the right, but not the obligation, to commence a suit or take action to enforce the applicable Takeda Patent against such Third Party perpetrating such infringement at its sole cost and expense. Each Party shall provide to the Party enforcing any such rights under this Section 9.5(c) reasonable assistance in such enforcement, at such enforcing Party's request, including joining such action as a party plaintiff if required by applicable Law to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider the other Party's comments on any such efforts. Any recoveries by a Party proceeding hereunder shall be [ \* ].

(d) **Settlement.** Takeda shall not settle any claim, suit or action that it brings under this Section 9.5 involving Affymax Patents (excluding Joint Patents) in any manner that would negatively impact Affymax Patents anywhere in the world, or that would limit or restrict the ability of either Party to manufacture, use, sell, offer for sale or import the Product anywhere

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in the world, without the prior written consent of Affymax. Affymax shall not settle any claim, suit or action that it brings under this Section 9.5 involving Takeda Patents (excluding Joint Patents) in any manner that would negatively impact the Takeda Patents or that would limit or restrict the ability of either Party to manufacture, use, sell, offer for sale or import the Product anywhere in the world, without the prior written consent of Takeda. Neither Party shall settle any claim, suit or action that it brings under this Section 9.5 involving Joint Patents in any manner that would negatively impact the Joint Patents or that would limit or restrict the ability of either Party to manufacture, use, sell, offer for sale or import the Product anywhere in the world, without the prior written consent of such other Party.

#### **9.6 Infringement of Third Party Rights in the Licensed Territory.**

(a) **Notice.** If any Product manufactured, used or sold by either Party, its Affiliates, licensees or sublicensees becomes the subject of a Third Party's claim or assertion of infringement of a Patent granted by a jurisdiction within the Licensed Territory relating to the manufacture, use, sale, offer for sale or importation of Hematide, Peptide[ \* ] or the Product, the Party first having notice of the claim or assertion shall promptly notify the JSC, and the Parties shall promptly meet to consider the claim or assertion and the appropriate course of action for an approval by the JSC.

(b) **Defense.** The Parties, working through the JSC, shall cooperate to defend any such claims under the strategy, terms and conditions as may be authorized by the JSC. The JSC shall designate one Party as the leading Party for such defense. The Parties shall make decisions with regard to such actions covered by this Section 9.6 jointly through the JSC in accordance with the provisions of Sections 2.5(b) and 2.5(c), provided that any unresolved disputes shall not be subject to settlement by expedited arbitration and, in the case of any unresolved dispute, each Party named as a defendant in such action shall be entitled upon written notice to defend itself in such matter independently by counsel of its own choice and at its own expense; provided, that each Party shall inform the other Party of the progress of such defense and, if reasonably requested by the other Party, shall reasonably cooperate with the other Party. For so long as the Parties continue to pursue such matter jointly through the JSC, all costs and expenses of any defense actions under this Section 9.6(b) shall be [ \* ]. In any action pursued jointly by the Parties through the JSC, the non-leading Party shall reasonably cooperate with the leading Party, including if required to conduct such defense, furnishing a power of attorney. The non-leading Party shall have the right to confer, through the JSC, with the leading Party in any such defense and the leading Party shall consider in good faith such input from the non-leading Party. If either Party desires to be released from the cost-sharing obligation described above, then such Party (a "**Removed Party**") shall be entitled, upon [ \* ] prior written notice to the JSC, to be released from sharing such costs and the matter shall thereafter be handled and pursued at the discretion of the continuing Party (a "**Continuing Party**"). Following the end of such [ \* ] notice period, the Continuing Party shall bear all costs and expenses for the continuation of the matter. The Removed Party shall promptly and reasonably cooperate to support the defense efforts of the Continuing Party. In any event, the Removed Party shall forego its rights to separate representation in any matter from which it has withdrawn.

(c) **Settlement.** Neither Party shall enter into any settlement of any claim described in this Section 9.6 that affects the other Party's rights or interests without such other

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Party's written consent, which consent shall not be unreasonably withheld or delayed.

**(d) Settlement Payment.** Any amounts that either Party becomes obligated to pay as a result of any settlement of or decision rendered in any defense pursuant to this Section 9.6 with respect to the manufacture, use, sale, offer for sale or import of the Product in or for the Licensed Territory shall be [ \* ] and [ \* ] as provided in Section [ \* ].

**9.7 Patent Marking.** Takeda (or its Affiliate, sublicensee or distributor) shall mark Product marketed and sold by Takeda (or its Affiliate, sublicensee or distributor) hereunder with appropriate patent numbers or indicia at Affymax's request to the extent permitted by applicable Law, if such markings or such notices impact recoveries of damages or equitable remedies available with respect to infringements of patents in the Licensed Territory.

**9.8 Infringement of Trademarks by Third Parties.** Affymax shall take all reasonable and appropriate steps to protect, defend and maintain each Product Trademark for use in connection with a Product, and all registrations therefor. Each Party shall notify the other Party promptly upon learning of any actual, alleged or threatened infringement of the Product Trademark. Upon learning of such actual, alleged or threatened infringement, Affymax shall have the obligation to, in consultation with Takeda, institute and control an appropriate action or proceeding to halt the infringement, unless the Parties otherwise mutually agree. All recoveries in connection therewith shall be allocated first to the costs and expenses of Affymax, and second, to the costs and expenses (if any) of Takeda, with any remaining amounts (if any) to be allocated as follows: (i) any recovery with respect to a country in the Royalty Territory shall be shared equally, and (ii) any recovery with respect to the U.S. shall be included in U.S. Product Profits for the applicable Fiscal Year. Takeda shall have the right to participate in all such actions or proceedings. For the purposes of the foregoing provisions of this Section 9.8, Affymax shall also have the right to control settlement of such claim; provided, however, that no settlement shall be entered into without the written consent of Takeda, not to be unreasonably withheld, conditioned or delayed if the Commercialization of the Product is not adversely impacted by the settlement. With regard to any other actual, alleged or threatened infringement by a Third Party of trade dress, logo, slogan, or of any unfair trade practices, trade dress imitation, passing off of counterfeit goods, or like offenses in relation to the Product, each Party shall notify the other Party promptly upon learning of the same, and, the JSC shall without delay consider and decide whether and what action should be taken against thereto.

**9.9 Patent Oppositions and Other Proceedings.** If either Party desires to bring an opposition, action for declaratory judgment, nullity action, interference, declaration for non-infringement, reexamination or other attack upon the validity, title or enforceability of a Patent owned or controlled by a Third Party that covers, in the Licensed Territory, the Peptide, [ \* ] or the Product, or the manufacture, use, sale, offer for sale or importation of the Peptide[ \* ] or the Product (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, a Third Party's claim or assertion of infringement under Section 9.6, in which case the provisions of Section 9.6 shall govern), such Party shall so notify the JSC and the Parties shall promptly confer to determine whether to bring such action or the manner in which to settle such action for the approval by the JSC. The Parties working jointly through the JSC shall cooperate to assert any such claims under the strategy, terms and conditions as may be authorized by the JSC. The JSC shall designate one Party as the leading Party for such claims.

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The Parties shall make decisions jointly through the JSC in accordance with the provisions of Sections 2.5(b) and 2.5(c), provided that any unresolved disputes shall not be subject to settlement by expedited arbitration and, in the case of any unresolved dispute, each Party shall be entitled to bring such action or settlement thereof independently by counsel of its own choice and at its own expense; provided, that each Party shall inform the other Party of the progress of such action and, if reasonably requested by the other Party, shall reasonably cooperate with the other Party. For so long as the Parties continue to pursue such matter jointly through the JSC, all costs and expenses of any actions or settlement efforts under this Section 9.9 shall be shared equally by the Parties. In any action pursued jointly by the Parties through the JSC, the non-leading Party shall cooperate fully with the leading Party, including, if required, to conduct such defense, furnishing a power of attorney. The non-leading Party shall have the right to confer with the leading Party, and the leading Party shall consider in good faith input from the non-leading Party. If either Party desires to be released from the cost-sharing obligation described above, then such Party (a “**Removed Party**”) shall be entitled, upon [ \* ] prior written notice to the JSC, to be released from sharing such costs and the matter shall thereafter be handled and pursued at the discretion of the continuing Party (a “**Continuing Party**”). Following the end of such [ \* ] notice period, the Continuing Party shall bear all costs and expenses for the continuation of the matter. The Removed Party shall promptly and reasonably cooperate to support the defense efforts of the Continuing Party. In any event, the Removed Party shall forego its rights to separate representation in any matter from which it has withdrawn. Any awards or amounts received in bringing any such action, if any, shall (a) if obtained through an action pursued jointly by the Parties through completion, shall be first allocated to reimburse the Parties’ respective expenses in such action, and any remaining amounts shall be [ \* ]; or (b) if obtained by a Continuing Party, shall be [ \* ].

**9.10 Parties’ Patent Rights.** If an Affymax Patent, Joint Patent or Takeda Patent becomes the subject of any proceeding commenced by a Third Party within the Licensed Territory in connection with an opposition, reexamination request, action for declaratory judgment, nullity action, interference or other attack upon the validity, title or enforceability thereof (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, an action for infringement against a Third Party under Section 9.5, in which case the provisions of Section 9.5 shall govern), then the Party owning or otherwise Controlling such Patent shall promptly notify the other Party of such effect and discuss with the other Party how to defend such proceedings. The Party owning or otherwise Controlling such Patent shall, in close communication and discussion with the other Party, control such defense and shall solely bear the costs of such defense; *provided* that if such action relates to a Joint Patent, the Parties shall confer and determine which Party shall control such action and bear the associated costs. The controlling Party shall permit the non-controlling Party to participate in the proceeding to the extent permissible under applicable Law, and to be represented by its own counsel in such proceeding, at the non-controlling Party’s expense. Any awards or amounts received in defending any such Third-Party action, if any, shall be first allocated to reimburse the Parties’ respective expenses in such action, and any remaining amounts shall be [ \* ].

**9.11 Orange Book Listing, Compendial Listing.** Upon request of Takeda, Affymax shall file appropriate information with the Regulatory Authority in the U.S. listing any Affymax Patents in the Orange Book and shall allow Takeda to file appropriate information with the

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Regulatory Authority in the Royalty Territory listing any Affymax Patents in the Orange Book equivalent in such Royalty Territory, if any, as a Patent related to the Product and the Parties shall use Diligent Efforts to obtain and maintain such listing.

**9.12 Registration of Exclusive License.** Within a reasonable period of time after the Effective Date, Affymax shall register before the Governmental Authorities in the Licensed Territory that Takeda is the exclusive licensee under the Affymax Patents pursuant to this Agreement.

**9.13 Certain Patent Matters.** With regard to [ \* ] set forth in [ \* ] including any matters derived from or related thereto (collectively the [ \* ]"), Affymax shall keep [ \* ], and shall [ \* ] where practicable and to the extent consistent with Affymax's [ \* ]; provided, however, that Affymax [ \* ] [ \* ] that would [ \* ] in Hematide, the Peptide, [ \* ] and the Product. Notwithstanding anything to the contrary in this Agreement, Affymax shall be [ \* ] of the [ \* ] at [ \* ], and the [ \* ] associated with the [ \* ] with respect to the Development and Commercialization of the Product in the Licensed Territory hereunder shall be [ \* ] in accordance with [ \* ]; provided, that any [ \* ] Affymax [ \* ] shall [ \* ], and [ \* ], shall be [ \* ].

## ARTICLE 10

### REPRESENTATIONS AND WARRANTIES

**10.1 Mutual Representations and Warranties.** Each Party hereby represents, warrants, and covenants (as applicable) to the other Party as follows:

(a) **Corporate Existence and Power.** It is a company or corporation duly organized, validly existing, and in good standing under the Laws of the jurisdiction in which it is incorporated, and has full corporate power and authority and the legal right to own and operate its property and assets and to carry on its business as it is now being conducted and as contemplated in this Agreement, including, without limitation, the right to grant the licenses granted by it hereunder.

(b) **Authority and Binding Agreement.** As of the Effective Date, (i) it has the corporate power and authority and the legal right to enter into this Agreement and perform its obligations hereunder; (ii) it has taken all necessary corporate action on its part required to authorize the execution and delivery of the Agreement and the performance of its obligations hereunder; and (iii) the Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid, and binding obligation of such Party that is enforceable against it in accordance with its terms.

(c) **No Conflict.** It is not a party to any agreement that would prevent it from granting the rights granted to the other Party under this Agreement or performing its obligations under this Agreement. The execution, delivery and performance of this Agreement shall not violate, conflict with or constitute a default under any agreement (including its corporate charter or other organizational documents) to which it is a party or to which it may be bound, or to its best knowledge, any applicable Laws or order of any court or other tribunal.

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(d) **No Debarment.** In the course of the Development and Commercialization of the Product, each Party has not used and shall not use, during the term of this Agreement, any employee or consultant who has been debarred by any Regulatory Authority, or is the subject of debarment proceedings by a Regulatory Authority.

**10.2 Additional Representations, Warranties and Covenants of Affymax.** Affymax represents, warrants and covenants (as applicable) to Takeda as follows, as of the Effective Date:

(a) **Regulatory Materials and Studies.** To the best of Affymax's knowledge, all Regulatory Materials Controlled by Affymax in existence as of the Effective Date and to which Takeda has rights of use or reference hereunder (collectively, "**Affymax Regulatory Materials**"), including the Regulatory Materials described in Section 4.1(a), have been prepared, maintained and retained in accordance with applicable Laws. All preclinical and clinical studies conducted with respect to Hematide and the Product in connection with the preparation of the Affymax Regulatory Materials, including such studies from which the data described in Section 4.1(a) are derived, have been conducted substantially in accordance with applicable Laws by persons with appropriate education, knowledge and experience. Affymax has not been debarred and is not subject to debarment, in each case pursuant to Section 306 of the FD&C Act or any similar law or regulation in any jurisdiction outside the United States.

(b) **Sufficiency of License Grants.**

(i) Except as set forth on Schedule 10.2(b)(i) hereto, the Affymax Patents, Affymax House Marks and Product Trademark are not subject to any encumbrance, lien or claim or ownership by any Third Party that is inconsistent with the rights and (sub)licenses granted to Takeda hereunder;

(ii) Except as set forth on Schedule 10.2(b)(ii) hereto, Affymax owns or possesses adequate right, title and interest in any Affymax Patents, Affymax House Marks and Product Trademark to grant the license thereto to Takeda as provided in Article 6;

(iii) No claim or litigation has been brought or, to the knowledge of Affymax, is threatened to be brought, by any person or entity alleging that (A) any of the Affymax Patents, Affymax House Marks and Product Trademark in the Licensed Territory is invalid or unenforceable, or (B) practice of any of the Affymax Technology and the use of Affymax House Marks and the Product Trademark in the Licensed Territory infringes or otherwise conflicts or interferes with any intellectual property or proprietary right of any Third Party;

(iv) To the knowledge of Affymax, prior to the Effective Date, no Third Party has infringed or misappropriated any Affymax Technology, Affymax House Marks or the Product Trademark by making, using, importing, offering for sale or selling the Product, Hematide [ \* ] or any product containing the Peptide or [ \* ], and, as of the Effective Date, there is no actual or threatened infringement or misappropriation of the Affymax Technology, Affymax House Marks or the Product Trademark by any Third Party by making, using,

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importing, offering for sale or selling the Product, Hematide[ \* ] or any product containing the Peptide [ \* ]

(v) Except as set forth on Schedule 10.2(b)(v), to the knowledge of Affymax, neither (A) Takeda's exercise of its rights hereunder with respect to the Affymax Technology, Affymax House Marks and Product Trademark, nor (B) Affymax's or Takeda's Development or Commercialization of the Product in the Field and the Licensed Territory, shall infringe any Patent or other intellectual property right or other proprietary right of any Third Party;

(vi) This Agreement is consistent with all of the Third Party License Agreements in all respects and does not conflict with, violate, breach or otherwise give rise to a default by Affymax under, any term of each of the Third Party License Agreement;

(vii) Affymax has obtained any and all consents, if any, required from Third Parties for Affymax to enter into this Agreement and to grant to Takeda the licenses and other rights provided herein and has provided a copy of such consents to Takeda;

(viii) Affymax owns or possesses adequate right, title and interest in the Affymax Know-How to grant the license thereto to Takeda as provided in Article 6;

(ix) Exhibit I sets forth all license agreements existing as of the Effective Date to which Affymax is a party and under which Affymax has obtained a license from certain Third Parties relating to inventions necessary or useful for Development or Commercialization of the Product, the Peptide, Hematide [ \* ] in the Field and the Licensed Territory; and

(x) Exhibit I and Exhibit N set forth all payment obligation relating to the Existing Third Party License Agreement for which Takeda shall be obligated to bear.

(c) **Patent/House Mark/Trademark Matters in the Licensed Territory.** With respect to the Licensed Territory, and as of the Effective Date: (i) All registration, maintenance and renewal fees due in connection with each Affymax Patent, Affymax House Marks and Product Trademark have been paid in a timely manner, (ii) all documents required to be filed in order to maintain each Affymax Patent, Affymax House Marks and Product Trademark have been filed in a timely manner, (iii) no action has been taken that would constitute waiver, abandonment or any similar relinquishment of rights with respect to any Affymax Patent, Affymax House Marks and Product Trademark, and (iv) all relevant prior art known to the entity filing any patent application for any Affymax Patent, Affymax House Marks and Product Trademark has been presented to the relevant patent authority.

(d) **Supply of Bulk API or Finished Product by Affymax.** All Bulk API or the Finished Product supplied by Affymax to Takeda pursuant to this Agreement shall be manufactured, handled, stored by Affymax or its Third Party contract manufacture(s) in compliance with applicable Laws, including without limitation the GMP requirements.

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(e) **Listing of Backup Compounds.** The list set forth on Schedule 1.9 includes all Backup Compounds as of the Effective Date.

(f) **Cross-License Agreement.** In addition to the representation and warranty set forth in Section 10.1(c), to the knowledge of Affymax, the requirement described in clause (ii) of Section 6.7(a) above shall not have any negative impact on the Parties' rights and obligations under this Agreement, assuming that the Parties comply with the terms of this Agreement, and, there is no fact or indication that the Cross-License is going to or may be terminated.

**10.3 Additional Representation of Takeda.** Takeda hereby represents and warrants to Affymax that, as of the Effective Date,

(a) Neither Takeda nor its Affiliates, either on their own or in collaboration with a Third Party, are marketing, promoting, or selling in the Licensed Territory any product that includes or is comprised of an ESA for the prevention, treatment or amelioration of anemia in humans, and

(b) All Finished Product supplied by Takeda to Affymax for the Development pursuant to this Agreement shall be Finished Manufactured, handled, stored by Takeda or its Third Party contract manufacture(s) in compliance with applicable Laws, including without limitation the GMP requirements.

**10.4 Disclaimer.** Takeda understands that the Product is the subject of ongoing clinical research and development and that Affymax cannot assure the safety or usefulness of the Product. In addition, Affymax makes no warranties except as set forth in this Agreement concerning the Affymax Technology.

**10.5 No Other Representations or Warranties.** EXCEPT AS EXPRESSLY STATED IN THIS AGREEMENT, NO REPRESENTATIONS OR WARRANTIES WHATSOEVER, WHETHER EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NON-INFRINGEMENT, OR NON-MISAPPROPRIATION OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS, ARE MADE OR GIVEN BY OR ON BEHALF OF A PARTY. ALL REPRESENTATIONS AND WARRANTIES, WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE, ARE HEREBY EXPRESSLY EXCLUDED.

## ARTICLE 11

### INDEMNIFICATION

**11.1 Indemnification by Affymax.** Affymax shall defend, indemnify, and hold Takeda, its Affiliates, its sublicensees under this Agreement and their officers, directors, employees, and agents (the "**Takeda Indemnitees**") harmless from and against any and all Third Party claims, suits, proceedings, damages, expenses (including court costs and reasonable attorneys' fees and expenses), and recoveries, including product liability claims (collectively, "**Claims**") to the extent that such Claims arise out of, are based on, or result from (a) the

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Development, manufacture, storage, handling, use, promotion, sale, offer for sale, and importation of Hematide and/or the Product by or on behalf of Affymax or the Development activities conducted by or on behalf of Affymax, including without limitation the Development activities prior to or ongoing as of the Effective Date, subject to Section 11.3; (b) a breach of any of Affymax's representations, warranties, and obligations under the Agreement; or (c) the willful misconduct or negligent acts of Affymax, its Affiliates, or the officers, directors, employees, or agents of Affymax or its Affiliates. The foregoing indemnity obligation shall not apply if the Takeda Indemnitees fail to comply with the indemnification procedures set forth in Section 11.4, or to the extent that any Claim arises from, is based on, or results from (i) the Development, manufacture, storage, handling, use, promotion, sale, offer for sale, and importation of Hematide and/or Product by Takeda or its Affiliates, sublicensees, or distributors; (ii) a breach of any of Takeda's representations, warranties, and obligations under the Agreement; or (iii) the willful misconduct or negligent acts of Takeda or its Affiliates, or the officers, directors, employees, or agents of Takeda or its Affiliates.

**11.2 Indemnification by Takeda.** Takeda shall defend, indemnify, and hold Affymax, its Affiliates, its sublicensees under this Agreement and their officers, directors, employees, and agents (the "**Affymax Indemnitees**") harmless from and against any and all Claims to the extent that such Claims arise out of, are based on, or result from (a) the Development, manufacture, storage, handling, use, promotion, sale, offer for sale, and importation of Hematide and/or Product by Takeda or its Affiliates, sublicensees, or distributors, subject to Section 11.3; (b) a breach of any of Takeda's representations, warranties, and obligations under the Agreement; or (c) the willful misconduct or negligent acts of Takeda or its Affiliates, or the officers, directors, employees, or agents of Takeda or its Affiliates. The foregoing indemnity obligation shall not apply if the Affymax Indemnitees fail to comply with the indemnification procedures set forth in Section 11.4, or to the extent that any Claim arises from, is based on, or results from (i) the Development, manufacture, storage, handling, use, promotion, sale, offer for sale, and importation of Hematide and/or Product by or on behalf of Affymax or the Development activities conducted by or on behalf of Affymax, including without limitation the Development activities prior to or ongoing as of the Effective Date; (ii) a breach of any of Affymax's representations, warranties, and obligations under the Agreement; or (iii) the willful misconduct or negligent acts of Affymax, its Affiliates, or the officers, directors, employees, or agents of Affymax or its Affiliates.

**11.3 Indemnification for the Product in the U.S.** Each Party hereby agrees to defend, indemnify, and hold the other Party and its officers, directors, employees, and agents harmless from and against any and all Claims to the extent that such Claims arise out of, are based on, or result from the Development, manufacture, storage, handling, use, promotion, sale, offer for sale, and importation of the Product in the U.S., by the indemnifying Party or its Affiliates, sublicensees, or distributors, but only to the extent that such Claims (i) result from the negligence or willful misconduct of the indemnifying Party or its Affiliates, sublicensees, or distributors, (ii) do not result also from the negligence or willful misconduct of the Party seeking indemnification (or its Affiliates, sublicensees, or distributors); and (iii) are not Claims for which a Party indemnifies the other Party pursuant to the Supply Agreement, Co-Promotion Agreement or any other written agreement between the Parties in respect of the Product. The foregoing indemnity obligation shall not apply if the applicable indemnitees fail to comply with the

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indemnification procedures set forth in Section 11.4. Expenses relating to any other Claims resulting directly or indirectly from the manufacture, use, handling, storage, sale or other disposition of the Product in the U.S. shall be shared equally by the Parties at the time such expenses are required to be paid.

**11.4 Indemnification Procedures.** The Party claiming indemnity under this Article 11 (the “**Indemnified Party**”) shall give written notice to the Party from whom indemnity is being sought (the “**Indemnifying Party**”) promptly after learning of such Claim. In the event of a claim relating to the U.S., the Parties shall confer as to whether such claim would result in indemnification under Section 11.3 and in any event how to respond to the claim. The Indemnified Party shall provide the Indemnifying Party with reasonable assistance, at the Indemnifying Party’s expense, in connection with the defense of the Claim for which indemnity is being sought. The Indemnified Party may participate in and monitor such defense with counsel of its own choosing at its sole expense; provided, however, the Indemnifying Party shall have the right to assume and conduct the defense of the Claim with counsel of its choice. The Indemnifying Party shall not settle any claim without the prior written consent of the Indemnified Party, such consent not to be unreasonably withheld, unless the settlement involves only the payment of money. So long as the Indemnifying Party is actively defending the Claim in good faith, the Indemnified Party shall not settle any such Claim without the prior written consent of the Indemnifying Party. If the Indemnifying Party does not assume and conduct the defense of the Claim as provided above, (a) the Indemnified Party may defend against, and consent to the entry of any judgment or enter into any settlement with respect to the claim in any manner the Indemnified Party may deem reasonably appropriate (and the Indemnified Party need not consult with, or obtain any consent from, the Indemnifying Party in connection therewith), and (b) the Indemnifying Party shall remain responsible to indemnify the Indemnified Party as provided in this Article 11.

**11.5 Limitation of Liability.** NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, PUNITIVE, OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 11.5 IS INTENDED TO OR SHALL LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER SECTION 11.1 OR 11.2 OR 11.3, OR DAMAGES AVAILABLE FOR A PARTY’S BREACH OF SECTION 6.4 OR CONFIDENTIALITY OBLIGATIONS IN ARTICLE 12.

**11.6 Insurance.** Each Party shall procure and maintain insurance, including product liability and other appropriate insurance, adequate to cover its obligations hereunder and which are consistent with normal business practices of prudent companies similarly situated at all times during which any Product is being clinically tested in human subjects or commercially distributed or sold. It is understood that such insurance shall not be construed to create a limit of either Party’s liability with respect to its indemnification obligations under this Article 11. Each Party shall provide the other with written evidence of such insurance upon request. Each Party shall provide the other with written notice at least thirty (30) days prior to the cancellation, non-renewal or material change in such insurance or self-insurance which materially adversely affects the rights of the other Party hereunder.

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## ARTICLE 12

### CONFIDENTIALITY

**12.1 Confidentiality.** Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, each Party agrees that, for the Term and until the later of (i) [ \* ] of the Effective Date, or (ii) [ \* ] the expiration or termination of the Term, it shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided for in this Agreement any Confidential Information furnished to it by the other Party pursuant to this Agreement except for that portion of such information or materials that the receiving Party can demonstrate by competent written proof:

(a) was already known to the receiving Party or its Affiliate, other than under an obligation of confidentiality, at the time of disclosure by the other Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

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

(d) was disclosed to the receiving Party or its Affiliate by a Third Party without obligations of confidentiality with respect thereto; or

(e) was independently discovered or developed by the receiving Party or its Affiliate without the aid, application, or use of Confidential Information of the other Party; provided, however, that this exception shall not apply to information or materials consisting of data and results generated or resulting from Development activities with respect to the Peptide, [ \* ] Hematide or the Product, which information and materials shall be deemed Confidential Information of the Party who has developed such information or materials regardless of whether such information and materials were independently discovered or developed by the receiving Party or its Affiliate.

**12.2 Authorized Disclosure.** Each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary in the following situations:

(a) filing or prosecuting Patents as permitted in this Agreement;

(b) regulatory submissions and other filings with Governmental Authorities, including filings with the Securities and Exchange Commission;

(c) prosecuting or defending litigation or other proceedings or regulatory actions;

(d) complying with applicable Laws;

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(e) disclosure to its employees, agents, and consultants, and any Third Parties (including licensees or sublicensees with which a Party is Developing or Commercializing the Product) only on a need-to-know basis and solely as necessary in connection with the performance of this Agreement, provided that in each case the recipient of such Confidential Information must agree to be bound by similar obligations of confidentiality and non-use at least as equivalent in scope as those set forth in this Article 12 prior to any such disclosure; and

(f) disclosure of the material financial terms of this Agreement to any bona fide potential investor, investment banker, acquiror, merger partner, or other potential financial partner; provided that in connection with such disclosure, the disclosing Party shall use all reasonable efforts to inform each recipient of the confidential nature of such Confidential Information and shall cause each recipient of such Confidential Information to treat such Confidential Information as confidential.

Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to clause (a) through (d) of this Section 12.2, it shall, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use reasonable efforts to secure confidential treatment of such information. In any event, the Parties agree to take all reasonable action to avoid disclosure of Confidential Information hereunder.

### **12.3 Publicity; Terms of Agreement.**

(a) The Parties agree that the material terms of this Agreement are included within the Confidential Information of both Parties, subject to the special authorized disclosure provisions set forth below in this Section 12.3. The Parties have agreed to make a joint public announcement of the execution of this Agreement substantially in the form of the press release attached as Exhibit K on or after the Effective Date.

(b) After release of such press release, if either Party desires to make a public announcement concerning the material terms of this Agreement, such Party shall give reasonable prior advance notice of the proposed text of such announcement to the other Party for its prior review and approval (except as otherwise provided herein), such approval not to be unreasonably withheld. A Party commenting on such a proposed press release shall provide its comments, if any, within five (5) Business Days after receiving the press release for review. Affymax shall have the right to make a press release announcing the achievement of each milestone under this Agreement as it is achieved, and the achievements of Regulatory Approvals in the Licensed Territory as they occur, subject only to the review procedure set forth in the preceding sentence. In relation to Takeda's review of such an announcement, Takeda may make specific, reasonable comments on such proposed press release within the prescribed time for commentary, but shall not withhold its consent to disclosure of the information that the relevant milestone has been achieved and triggered a payment hereunder. Neither Party shall be required to seek the permission of the other Party to repeat any information regarding the terms of this Agreement that has already been publicly disclosed or previously agreed to by such Party, or by the other Party, in accordance with this Section 12.3.

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(c) The Parties acknowledge that Affymax may be obligated to file a copy of this Agreement with the U.S. Securities and Exchange Commission (the "SEC"). Affymax shall be entitled to make such a required filing, provided that it requests confidential treatment of certain commercial terms and sensitive technical terms hereof to the extent such confidential treatment is reasonably available to Affymax. In the event of any such filing, Affymax shall provide Takeda with a copy of the Agreement marked to show provisions for which Affymax intends to seek confidential treatment and shall reasonably consider and incorporate Takeda's comments thereon to the extent consistent with the legal requirements governing redaction of information from material agreements that must be publicly filed. Takeda shall promptly provide any such comments. Takeda recognizes that U.S. Laws and SEC policies and regulations to which Affymax is and may become subject may require Affymax to publicly disclose certain terms of this Agreement that Takeda may prefer not be disclosed, and that Affymax is, after completing the above mentioned procedures, entitled hereunder to make such required disclosures to the extent legally required.

**12.4 Publications.** Neither Party may publish peer reviewed manuscripts, or give other forms of public disclosure such as abstracts and presentations, of results of studies carried out under this Agreement with respect to the Licensed Territory, without the opportunity for prior review by the other Party. Each Party shall provide the other Party the opportunity to review and comment on any proposed manuscripts or presentations which relate to any Product at least [ \* ] prior to their intended submission for publication or presentation. Each Party shall consider the comments of the other Party and shall remove any and all of the other Party's Confidential Information at the request of such other Party. A Party seeking publication shall also provide the other Party a copy of the manuscript at the time of the submission. Neither Party shall have the right to publish or present the other Party's Confidential Information without the other Party's prior written consent, except as expressly permitted in this Agreement.

**12.5 Injunction.** Each Party shall be entitled, in addition to any other right or remedy it may have, at Law or in equity, to seek an injunction in any court of competent jurisdiction, enjoining or restraining the other Party or its Affiliates from any violation or threatened violation of this Article 12.

## ARTICLE 13

### TERM AND TERMINATION

**13.1 Term.** This Agreement shall become effective on the Effective Date and, unless earlier terminated pursuant to this Article 13, shall remain in effect in the Licensed Territory until the expiration of all of Takeda's payment obligations, including without limitation the U.S. Product Profit sharing under Article 8, on a country-by-country basis.

#### **13.2 Early Termination.**

(a) **Withdrawal by Takeda.** Takeda shall have the right to terminate this Agreement, in its entirety, upon written notice to Affymax by at least six (6) months' written notice prior to the effective date of termination; provided, that in no event shall the effective date of such termination precede the second anniversary of the Effective Date, and further provided,

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that Takeda shall have the right to terminate this Agreement even before the end of such two (2) year period if the Development of the Product in the Licensed Territory hereunder are terminated entirely for patient safety concerns or pursuant to a requirement imposed by the Regulatory Authorities in the Licensed Territory or by the external monitoring board. If Takeda terminates this Agreement pursuant to this Section 13.2(a), then:

(i) Takeda shall not, during the applicable notice period, take any action that could adversely affect or impair the further Development and Commercialization of the Product.

(ii) The JSC shall coordinate the wind-down of Takeda's efforts under this Agreement.

(iii) Takeda shall continue to be responsible for any payments that become due to Affymax pursuant to this Agreement that were incurred or accrued during the applicable notice period.

(iv) Only in case Takeda terminates this Agreement in its entirety pursuant to this Section 13.2(a) prior to the First Commercial Sale of the Product in the U.S. for other reasons than Technical Failure (as defined below), Takeda, within [ \* ] of delivery of such written termination notice, shall pay to Affymax a fee of [ \* ] by wire transfer of immediately available funds into an account designated by Affymax in writing. For the purpose of this Section, "Technical Failure" shall mean the case in which: (a) the Development of the Product in the Licensed Territory is discontinued entirely for patient safety concerns or pursuant to a requirement imposed by Regulatory Authorities in the Licensed Territory or by an external monitoring board or (b) the primary end point of the first pivotal Phase III Clinical Trial for the Dialysis CKD Anemia or the Pre-Dialysis CKD Anemia is not achieved. Such fee shall be non-refundable and non-creditable against any other payments due hereunder.

**(b) Termination for Breach.**

(i) Affymax shall have the right to terminate this Agreement upon written notice to Takeda if Takeda, after receiving written notice identifying such material breach by Takeda, fails to cure such material breach within ninety (90) days from the date of such notice (or within ten (10) Business Days notice in the event such material breach is solely based upon Takeda's failure to pay any amounts due Affymax hereunder); *provided*, that if such breach cannot be remedied within such 90-day period and Takeda has provided Affymax with a written plan, reasonably acceptable to Affymax, setting forth the activities to be performed by Takeda to remedy such breach, then Affymax may not terminate this Agreement during such time (not to exceed an additional ninety (90) days) as Takeda is diligently pursuing the performance of the activities described in the plan; and provided, further, that if such material breach relates solely to a particular country in the Licensed Territory, then Affymax may terminate this Agreement only with respect to the applicable country but may not terminate this Agreement with respect to any other countries.

(ii) Takeda shall have the right to terminate this Agreement upon written notice to Affymax if Affymax, after receiving written notice identifying a material breach

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by Affymax of its obligations under this Agreement, fails to cure such material breach within ninety (90) days from the date of such notice (or within ten (10) Business Days notice in the event such material breach is solely based upon Affymax's failure to pay any amounts due Takeda hereunder); provided, that if such breach cannot be remedied within such 90-day period and Affymax has provided Takeda with a written plan, reasonably acceptable to Takeda, setting forth the activities to be performed by Affymax to remedy such breach, then Takeda may not terminate this Agreement during such time (not to exceed an additional ninety (90) days) as Affymax is diligently pursuing the performance of the activities described in the plan; and provided, further, that if such material breach relates solely to a particular country in the Licensed Territory, then Takeda may terminate this Agreement only with respect to the applicable country but may not terminate this Agreement with respect to any other countries.

(iii) For clarity, if a Party elects not to exercise its rights to terminate this Agreement pursuant to this Section 13.2(b) for the other Party's uncured material breach, but instead elects to allow this Agreement to continue in effect, then the breaching Party shall continue to be liable to the other Party for any breach of representations, warranties, obligations or agreements made in this Agreement by such breaching Party, and the non-breaching Party shall be entitled to pursue legal and equitable remedies arising from such breach that are available to it.

**13.3 Other Remedies for Affymax Breach.** In addition to the termination remedy described in Sections 13.2(b), Takeda shall have certain other remedies for the material breaches of this Agreement by Affymax (which in all events shall be (i) in addition to, and not in lieu of, any other remedies available to Takeda under this Agreement or applicable law, and (ii) subject to the notice and cure provisions of Section 13.2(b)), specified as follows:

(a) **Supply.** The Supply Agreement shall provide Takeda with certain sufficient remedies (including, by way of example only, the right to obtain materials from a second source or to initiate a technology transfer) if Affymax materially breaches its obligation to deliver quantities of Bulk API pursuant to the terms thereof.

(b) **Regulatory.** If Affymax materially breaches its obligations to obtain or maintain Regulatory Materials with respect to the Product in accordance with the terms of this Agreement, then, upon request of Takeda, Affymax shall transfer and assign to Takeda or its designee the applicable Regulatory Materials or the right to obtain the applicable Regulatory Materials, as the case may be.

(c) **Continuing Right to Additional Product.** If Takeda otherwise has the right to terminate the entire Agreement pursuant to Section 13.2(b)(ii) due to a material breach by Affymax, Takeda shall have, in addition to its other remedies, the right to elect in writing to continue the Agreement pursuant to Section 13.2(b)(iii) only in order to retain its rights to the Additional Product pursuant to the terms of Section 3.12 until such time as Takeda determines whether to exercise its right to the first Additional Product either selected by Takeda or has achieved Proof of Concept but not been selected pursuant to Section 3.12. If Takeda exercises such right, then the Agreement shall be reinstated with respect to the Additional Product. If Takeda does not exercise such right, then the Agreement shall be deemed terminated.

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**13.4 Effect of Termination of the Agreement.** Upon termination by Affymax of the Agreement under Section 13.2(b), or upon termination by Takeda under Section 13.2(a), the following shall apply (in addition to any other rights and obligations under Section 13.5, 13.6 or 13.7 or otherwise under this Agreement with respect to such termination) with respect to the affected territory or territories:

(a) **Partial Termination.** In the event of a termination by Affymax under Section 13.2(b) for a particular country, such country shall be deemed excluded from the definition of Licensed Territory.

(b) **Regulatory Materials.** To the extent permitted by applicable Law, Takeda shall transfer and assign to Affymax all Regulatory Materials and Regulatory Approvals for Product for the terminated country(ies) of the Licensed Territory that are Controlled by Takeda, and shall grant Affymax a right of reference to all Regulatory Materials filed by Takeda in the Licensed Territory solely for the purpose of Affymax obtaining Regulatory Approval for the Product in such terminated country(ies).

(c) **Takeda License.** Takeda hereby grants to Affymax, effective only in the event of termination described in this Section 13.4 above and only to the extent such license is practicable and available, a non-exclusive, worldwide, fully-paid, royalty-free license, with the right to grant multiple tiers of sublicenses, under the Licensed Takeda Technology (as defined below) existing as of the date of such termination to develop, make, have made, use, sell, offer for sale, and import Bulk API[ \* ] and the Product in or for the terminated country(ies) of the Licensed Territory; provided, that with respect to any Takeda Patent that was assigned by Affymax to Takeda pursuant to the terms of Section 9.3 (“**Former Affymax Patent**”), such license may be used for any purpose whatsoever. For clarity, this Section 13.4(c) shall not oblige Takeda to maintain any of the Takeda Patents in any country, in spite of the license granted to Affymax; provided, that after such termination, if Takeda is requested by Affymax to assign to Affymax any Patent included in the Licensed Takeda Technology and if Takeda still maintains such Patent at that time and decides in its reasonable discretion that it is able to assign such Patent to Affymax, then Takeda shall assign such Patent to Affymax, conditioned upon the covenant not to sue set forth below (any Patent so assigned, an “**Assigned Takeda Patent**”). Takeda hereby covenants not to sue Affymax and its sublicensees under this Agreement, effective only in the event of termination described in this Section 13.4 above, under any Takeda Patent (other than the Licensed Takeda Technology for which a license or assignment has been made above) existing as of the date of such termination, for activities to develop, make, have made, use, sell, offer for sale, and import Bulk API[ \* ], Backup Compounds (as of the date of such termination) and the Product in or for the terminated country(ies) of the Licensed Territory. Affymax hereby covenants not to sue Takeda, its Affiliates, and their sublicensees, effective immediately after the assignment to Affymax of an Assigned Takeda Patent, under any such Assigned Takeda Patent, for any activities and for any purposes whatsoever. As used in this provision, “**Licensed Takeda Technology**” means, collectively, (i) any Former Affymax Patent, and (ii) any Takeda Technology made by Takeda’s employees, agents, or independent contractors in the course of conducting its activities under this Agreement.

(d) **Transition Assistance.** Takeda shall, for a reasonable period of time, provide such assistance, at no cost to Affymax, to transfer or transition to Affymax all other

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technology or know-how, or then-existing commercial arrangements, that is, or are, reasonably necessary or useful for Affymax to commence or continue Developing, conducting Finished Manufacturing of or Commercializing the Product in or for the terminated country(ies) of the Licensed Territory, to the extent Takeda is then performing or having performed such activities, including without limitation transferring, upon request of Affymax, any agreements or arrangements with Third Party suppliers or vendors to supply or sell the Product in such country(ies) of the Licensed Territory, to the extent practicable. If any such contract between Takeda and a Third Party for the supply of Bulk API or Finished Product for such terminated country(ies) of the Licensed Territory is not assignable to Affymax, then Takeda shall reasonably cooperate with Affymax to arrange to continue to obtain such supply from such entity, and Takeda shall supply such Bulk API or Finished Product, as applicable, to Affymax, at a cost that equals [ \* ] (calculated in a manner consistent with the definition of [ \* ] for a reasonable period. In addition, to the extent that Takeda or its Affiliate is then manufacturing Bulk API or Finished Product for the other country(ies) than such terminated country(ies) of the Licensed Territory, Takeda shall continue to manufacture, and shall supply to Affymax, at a cost that equals [ \* ] (calculated in a manner consistent with the definition of [ \* ], such Bulk API or Finished Product for Affymax's use in such terminated country(ies) of the Licensed Territory for a reasonable period in order to permit Affymax to establish sufficient manufacturing capacity for Bulk API or Finished Product for such terminated country(ies) of the Licensed Territory. Such period shall be no more than [ \* ] unless otherwise agreed by the Parties.

(e) **Remaining Inventories.** Affymax shall have the right to purchase from Takeda all of the inventory of Bulk API or Finished Product held by Takeda for such terminated country(ies) as of the effective date of termination of this Agreement at a price equal to [ \* ] for such terminated country(ies). Affymax shall notify Takeda within [ \* ] after the date of termination of the Agreement whether Affymax elects to exercise such right. If Affymax does not exercise such right, then Takeda shall have the right to sell in such terminated country(ies) of the Licensed Territory any such remaining inventory over a period of no greater than [ \* ] after the effective date of termination of this Agreement.

(f) **Termination of Licenses.** For clarity, upon any termination of this Agreement under Section 13.2, the licenses granted to Takeda under this Agreement for such terminated country(ies) shall terminate.

(g) **Restriction on Licensing of Compounds.** If Takeda terminates this Agreement pursuant to Section 13.2(a) upon the discontinuation of Development of the then-current Product and failure by the Parties to agree on a Replacement Product Candidate to replace it under Section 3.9, then, during the [ \* ] period following the effective date of such termination, Affymax shall not license any Replacement Product Candidate to any Third Party for development or commercialization for the prevention, treatment or amelioration of anemia. If Affymax desires to license any such Replacement Product Candidate, then Affymax shall provide Takeda with a right of first negotiation to such license under terms and conditions corresponding to those set forth in Section 3.9.

**13.5 Effects of Expiration.** Following expiration of the Term pursuant to Section 13.1, Takeda shall have a fully paid non-exclusive license under the Affymax Technology to make, have made, use, sell and import the Product in the Licensed Territory, under any

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trademark or trademarks other than the Product Trademark owned or Controlled by Takeda. In addition, in the event Takeda desires to continue to purchase Bulk API from Affymax, it shall so notify Affymax no later than [ \* ] prior to the expiration of this Agreement, and thereafter Affymax shall, in its sole discretion, either (a) continue to supply Bulk API at a cost equal to the Manufacturing Cost plus [ \* ] for a period to be negotiated by the Parties, or (b) permit Takeda to manufacture itself, or on its behalf through a contract supplier, Bulk API, and in such event grant to Takeda a non-exclusive royalty-free license, under Affymax Technology related to manufacture of Bulk API, and otherwise assist Takeda to enable it to obtain continuous supply of Bulk API, including without limitation, providing relevant documents and using Diligent Efforts to encourage or cause Affymax's then-current Third Party contract manufacturers of Bulk API to manufacture and supply to Takeda such Bulk API directly. Upon request of Takeda, Affymax shall provide to Takeda reasonable access to Affymax's manufacturing personnel to facilitate the foregoing efforts on terms to be agreed upon by the Parties.

**13.6 Other Remedies.** Termination or expiration of this Agreement for any reason shall not release any Party from any liability or obligation that already has accrued prior to such expiration or termination, nor affect the survival of any provision hereof to the extent it is expressly stated to survive such termination. Termination or expiration of this Agreement for any reason shall not constitute a waiver or release of, or otherwise be deemed to prejudice or adversely affect, any rights, remedies or claims, whether for damages or otherwise, that a Party may have hereunder or that may arise out of or in connection with such termination or expiration.

**13.7 Rights in Bankruptcy.** All rights and licenses granted under or pursuant to this Agreement by Affymax are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that Takeda, as licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the U.S. Bankruptcy Code. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against Affymax under the U.S. Bankruptcy Code, Takeda shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, which, if not already in Takeda's possession, shall be promptly delivered to it (a) upon any such commencement of a bankruptcy proceeding upon Takeda's written request therefor, unless Affymax elects to continue to perform all of its obligations under this Agreement or (b) if not delivered under clause (a), following the rejection of this Agreement by Affymax upon written request therefor by Takeda.

**13.8 Survival.** The following provisions shall survive any expiration or termination of this Agreement for the period of time specified therein (or, if no such period is specified, indefinitely): Articles 1, 11 (other than Section 11.6), 12, 14, and 15, and Sections 5.7 (but only the last sentence thereof), 5.11 (to the extent that Takeda uses a Product Trademark after such expiration or termination), 7.4, 8.11, 9.1, 9.8 (to the extent that Takeda uses a Product Trademark after such expiration or termination), 10.4, 10.5, 13.4, 13.5, 13.6, 13.7, and 13.8.

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## ARTICLE 14

### DISPUTE RESOLUTION

**14.1 English Language; Governing Law.** This Agreement was prepared in the English language, which language shall govern the interpretation of, and any dispute regarding, the terms of this Agreement. This Agreement and all disputes arising out of or related to this Agreement or any breach hereof shall be governed by and construed under the Laws of the State of New York, without giving effect to any choice of law principles that would require the application of the Laws of a different state.

#### **14.2 Disputes.**

(a) The Parties recognize that disputes as to certain matters may from time to time arise during the Term which relate to either Party's rights or obligations hereunder. It is the objective of the Parties to establish procedures to facilitate the resolution of disputes arising under this Agreement in an expedient manner by mutual cooperation and without resort to litigation. To accomplish this objective, the Parties agree to follow the procedures set forth in this Section 14.2 to resolve any controversy or claim arising out of, relating to or in connection with any provision of this Agreement, if and when a dispute arises under this Agreement. With respect to all disputes arising between the Parties (other than those matters delegated to the JSC, which shall be governed in accordance with Section 2.5(c)), including, without limitation, any alleged failure to perform, or breach, of this Agreement, or any issue relating to the interpretation or application of this Agreement, if the Parties are unable to resolve such dispute within [ \* ] after such dispute is first identified by either Party in writing to the other, the Parties shall refer such dispute to the senior executive officers for each Party for attempted resolution by good faith negotiations within [ \* ] after such notice is received. If the senior executive officers designated by the Parties are not able to resolve such dispute within such [ \* ] period, either Party may submit such dispute in accordance with Section 14.2(b).

(b) If a dispute is not resolved as provided in the preceding Section 14.2(a), any claim or controversy of whatever nature arising out of or relating to this Agreement or any breach hereof shall be brought exclusively in a court of competent jurisdiction, federal or state, located in San Francisco, California, and in no other jurisdiction. Each Party hereby consents to personal jurisdiction and venue in, and agrees to service of process issued or authorized by, such court.

(c) Notwithstanding anything to the contrary in this Article 14, either Party may seek injunctive relief in any court in any jurisdiction where appropriate.

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## ARTICLE 15

### MISCELLANEOUS

**15.1 Entire Agreement; Amendment.** This Agreement, including the Exhibits hereto, sets forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Effective Date, all prior agreements and understandings between the Parties with respect to the subject matter hereof. Notwithstanding anything to the contrary herein, the Parties agree that nothing in this Agreement shall be construed to terminate, modify, amend or supersede the Japan Collaboration Agreement. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth herein and therein. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

**15.2 Force Majeure.** Both Parties shall be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by force majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse shall be continued so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. For purposes of this Agreement, force majeure shall include conditions beyond the control of the Parties, including without limitation, an act of God, war, civil commotion, terrorist act, labor strike or lock-out, epidemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe, and failure of plant or machinery (provided that such failure could not have been prevented by the exercise of skill, diligence, and prudence that would be reasonably and ordinarily expected from a skilled and experienced person engaged in the same type of undertaking under the same or similar circumstances). Notwithstanding the foregoing, a Party shall not be excused from making payments owed hereunder because of a force majeure affecting such Party.

**15.3 Notices.** Any notice required or permitted to be given under this Agreement shall be in writing, shall specifically refer to this Agreement, and shall be addressed to the appropriate Party at the address specified below or such other address as may be specified by such Party in writing in accordance with this Section 15.3, and shall be deemed to have been given for all purposes (a) when received, if hand-delivered sent by a reputable overnight delivery service, or by facsimile (with electronic confirmation of receipt), or (b) seven (7) days after mailing, if mailed by first class certified or registered mail, postage prepaid, return receipt requested.

If to Affymax:           Affymax, Inc.  
4001 Miranda Avenue  
Palo Alto, California 94306  
Attn: Chief Executive Officer

With a copy to: Barbara A. Kosacz, Esq.  
Cooley Godward LLP  
5 Palo Alto Square  
3000 El Camino Real  
Palo Alto, CA 94306

If to Takeda: Takeda Pharmaceutical Company Limited  
1-1, Doshomachi 4-chome, Chuo-ku,  
Osaka, 540-8645, Japan  
Attn: General Manager, Global Licensing and Business Development

**15.4 No Strict Construction; Headings.** This Agreement has been prepared jointly and shall not be strictly construed against either Party. Ambiguities, if any, in this Agreement shall not be construed against any Party, irrespective of which Party may be deemed to have authored the ambiguous provision. The headings of each Article and Section in this Agreement have been inserted for convenience of reference only and are not intended to limit or expand on the meaning of the language contained in the particular Article or Section.

**15.5 Assignment.** Neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other, except that a Party may make such an assignment without the other Party's consent to Affiliates or to a successor to substantially all of the business of such Party in the field to which this Agreement relates, whether in a merger, sale of stock, sale of assets or other transaction. Notwithstanding the definitions of Affymax Technology or Takeda Technology in Article 1, in the event of such transaction, however, intellectual property rights of the acquiring party to such transaction (if other than one of the Parties to this Agreement) shall not be included in the Affymax Technology or Takeda Technology, as the case may be, licensed to the other Party hereunder to the extent held by such acquiror prior to such transaction, or to the extent such technology is developed outside the scope of activities conducted with respect to the Peptide[ \* ] Hematide, an ESA, Backup Compound or Product. Any permitted successor or assignee of rights or obligations hereunder shall, in writing to the other Party, expressly assume performance of such rights or obligations. Any permitted assignment shall be binding on the successors of the assigning Party. Any assignment or attempted assignment by either Party in violation of the terms of this Section 15.5 shall be null, void and of no legal effect.

**15.6 Performance by Affiliates.** Each Party may discharge any obligations and exercise any right hereunder through any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement shall be deemed a breach by such Party, and the other Party may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

**15.7 Further Actions.** Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

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**15.8 Severability.** If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by any court of competent jurisdiction from which no appeal can be or is taken, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions hereof. The Parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

**15.9 No Waiver.** Any delay in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement, except with respect to an express written and signed waiver relating to a particular matter for a particular period of time.

**15.10 Independent Contractors.** Each Party shall act solely as an independent contractor, and nothing in this Agreement shall be construed to give either Party the power or authority to act for, bind, or commit the other Party in any way. Nothing herein shall be construed to create the relationship of partners, principal and agent, or joint-venture partners between the Parties.

**15.11 Counterparts.** This Agreement may be executed in one (1) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement shall be binding upon the delivery by each Party of an executed signature page to the other Party by facsimile transmission. If signature pages are so delivered by facsimile transmission, each Party shall also immediately deliver an executed original counterpart of this Agreement to the other Party by courier delivery service.

**15.12 Construction.** Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders, and the word "or" is used in the inclusive sense (and/or). The captions of this Agreement are for convenience of reference only and in no way define, describe, extend or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The term "including" as used herein means including, without limiting the generality of any description preceding such term. References to "Article," "Section" or "Exhibit" are references to the numbered sections of this Agreement and the exhibits attached to this Agreement, unless expressly stated otherwise.

**[Signature page follows.]**

**IN WITNESS WHEREOF**, the Parties have executed this Agreement in duplicate originals by their duly authorized officers as of the Effective Date.

**TAKEDA PHARMACEUTICAL COMPANY LIMITED    AFFYMAX, INC.**

By: /s/ Yasuchika Hasegawa

By: /s/ Arlene Morris

Name: Yasuchika Hasegawa

Name: Arlene Morris



Title: President & COO

Title: President & CEO

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**PATENT**  
**REEL: 018375 FRAME: 0572**

**EXHIBIT A**  
**AFFYMAX HOUSE MARKS**

AFFYMAX	United States	Registration No. 1,855,403
(black/white)  AFFYMAX	United States	Serial No. 76/468,006
(color)  AFFYMAX	United States	Serial No. 76/468,005

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## **EXHIBIT B**

### **AFFYMAX PATENTS**

To the extent the following table lists patents and patent applications filed or issued in the United States, Affymax Patents shall include any equivalent applications and patents that are or will be filed with patent authorities in the Licensed Territory (*i.e.*, those applications and patents that claim priority to such United States applications or to the applications from which such United States patents issued).

[ \* ]

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**EXHIBIT C**

**[ \* ] STRUCTURE**

**[ \* ]**

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**PATENT  
REEL: 018375 FRAME: 0575**

**EXHIBIT D**  
**PEPTIDE STRUCTURE**

[ \* ]

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**PATENT**  
**REEL: 018375 FRAME: 0576**

**EXHIBIT E**

**REAGENT**

[ \* ]

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## **EXHIBIT F**

### **JSC MEMBERS AND ALLIANCE REPRESENTATIVES**

**For Affymax:**

**JSC Members:**

[ \* ]

**Alliance Representative:**

[ \* ]

**For Takeda:**

**JSC Members:**

[ \* ]

**Alliance Representative:**

[ \* ]

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## **EXHIBIT G**

**[ \* ]**

**[ \* ]**

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**PATENT  
REEL: 018375 FRAME: 0579**

**EXHIBIT H**  
**U.S. DEVELOPMENT PLAN**  
{Entire Exhibit H is redacted}

## **EXHIBIT I**

[ \* ]

[ \* ]

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**PATENT**  
**REEL: 018375 FRAME: 0581**

## EXHIBIT J

### FINANCIAL DEFINITIONS

The following sets forth the definitions of cost and expense categories included in Commercial Expenses in amounts consistent with the Development Budget set forth in the U.S. Commercialization Plan.

#### 1. COST OF GOODS SOLD

**“Cost of Goods Sold”** means the cost of Finished Product packaged in final therapeutic form and Commercialized in the U.S., calculated as [ \* ] percent ([ \* ]) [ \* ] of the sum of: (a) the supply price from Affymax to Takeda of the Bulk API contained in such Finished Product (i.e., [ \* ]) (which [ \* ]); (b) the freight, postage, shipping, transportation, insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Bulk API; (c) Manufacturing Costs for the Finished Manufacture of the Finished Product; and (d) the freight, postage, shipping, transportation and insurance, warehousing and handling charges actually allowed or paid by Takeda with regard to such Finished Product.

All amounts shall be determined in accordance with generally accepted accounting principles, consistently applied. To the extent practical, the Parties shall use conforming systems for determining Cost of Goods Sold.

#### 2. MANUFACTURING COSTS

**“Manufacturing Costs”** means::

(a) With respect to Bulk API manufactured by the Third Party contract manufacturer(s) of Affymax, the amount of all payments that Affymax makes to such Third Party contract manufacturer(s) for supply and delivery of such Bulk API, plus all payments made to Third Party contractors for release and batch stability testing services for the Bulk API.

(b) With respect to Bulk API manufactured by Affymax, if any, Manufacturing Costs shall mean Direct Expenses and Indirect Expenses incurred by Affymax in, and reasonably allocable to, the manufacture of such Bulk. As used herein:

(i) “Direct Expenses” are those material and labor and services expenses captured in time sheets, invoices, and the like which are specifically attributable to manufacture of the Bulk API, including costs of raw materials, manufacturing supplies, solvents, containers, container components, packaging, labels and other printed materials used in production. Direct labor expenses include allocated salaries and fringe benefits for personnel directly involved in manufacturing Bulk API in accordance with cGMP requirements such as production, quality control, quality assurance, microbiology, and other similar departments as needed to the extent such personnel participate directly in the production of Bulk API and components thereof. Direct services expenses include reasonable out of pocket payments to Third Parties for services related to the manufacture of Bulk API or components thereof.

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(ii) “Indirect Expenses” include production indirect costs such as a reasonable allocation of expenses associated with Affymax personnel supporting directly the manufacturing of Bulk API in accordance with cGMP requirements. Indirect Expenses can include labor for and indirect costs of quality control, quality assurance, raw material acquisition and acceptance, microbiology, document control, calibration/validation, and non-R&D expenses for process development and analytical methods development, and shall not include any Direct Expenses.

For avoidance of doubt, any given cost included in Manufacturing Costs of Bulk API shall not be included more than once in any calculation described herein.

(c) With respect to Finished Product Finished Manufactured by the Third Party contract manufacturer(s) of Takeda, the amount of all payments that Takeda makes to such Third Party contract manufacturer(s) for such Finished Manufacture, plus all payments made to Third Party contractors for release and batch stability testing services for such Finished Product.

(d) With respect to Finished Product Finished Manufactured by Takeda, if any, Manufacturing Costs shall mean Direct Expenses and Indirect Expenses incurred by Takeda in, and reasonably allocable to, such Finished Manufacture. As used herein:

(i) “Direct Expenses” are those material and labor and services expenses captured in time sheets, invoices, and the like which are specifically attributable to the Finished Manufacture, including costs of raw materials (other than Bulk API), manufacturing supplies, solvents, containers, container components, packaging, labels and other printed materials used in production. Direct labor expenses include allocated salaries and fringe benefits for personnel directly involved in Finished Manufacturing in accordance with cGMP requirements such as production, quality control, quality assurance, microbiology, and other similar departments as needed to the extent such personnel participate directly in the production of Finished Product and components thereof (other than the Bulk API). Direct services expenses include reasonable out of pocket payments to Third Parties for services related to the Finished Product or components thereof (other than the Bulk API).

(ii) “Indirect Expenses” include production indirect costs such as a reasonable allocation of expenses associated with Takeda personnel supporting directly the Finished Manufacturing in accordance with cGMP requirements. Indirect Expenses can include labor for and indirect costs of quality control, quality assurance, raw material acquisition and acceptance, microbiology, document control, calibration/validation, and non-R&D expenses for process development and analytical methods development, and shall not include any Direct Expenses.

For avoidance of doubt, any given cost included in Manufacturing Costs of Finished Product shall not be included more than once in any calculation described herein.

### 3. PRE-MARKETING AND MARKETING EXPENSES

**“Pre-marketing Expenses”** shall mean expenses incurred by a Party, whether paid to a Third Party or incurred through internal resources, that are agreed to by the Parties through the JSC and are attributable to the marketing of the Product prior to the approval of the initial U.S. Commercialization Plan.

**“Marketing Expenses”** shall be the sum of Marketing Management, Market and Consumer Research, Advertising, Trade Promotion, Detailing Costs, Consumer Promotion, and Education Expenses (as each is described below), and all other costs attributable to the sales, promotion or marketing of a Finished Product in the U.S., all in accordance with the then-current U.S. Commercialization Plan.

**“Marketing Management”** shall include product management and sales promotion management compensation and related costs and department expenses, including product related public relations, relationships with opinion leaders and professional societies, health care economics studies, contract pricing and administration, market information systems, governmental affairs activities for reimbursement, formulary acceptance, sales meeting of the Sales Representatives, and other activities directly related to the marketing and/or promotion of the Finished Product for the Field in the U.S., management and administration of managed care and national accounts and other activities associated with developing overall sales and marketing strategies and planning for Finished Product in the U.S. In addition, payments to Third Parties in connection with the Product Trademark selection, filing, prosecution and enforcement in the U.S. shall be included in the Marketing Management. Such costs may be allocated among the Finished Product and other products of a Party on a percent of sales or other basis consistently applied within and across such Party’s operating units but such allocation is made no less favorable to the Finished Product than to the internal allocation to the Party’s other products.

**“Market and Consumer Research”** shall include compensation and departmental expenses for market and consumer research personnel and payments to Third Parties related to conducting and monitoring professional and consumer appraisals of Finished Product for the Field and for the U.S. market, such as market share services (*e.g.*, IMS data), pricing analysis, special research testing and focus groups. Expenditures not directly related to a Finished Product or the Field or U.S. market may be allocated among the Finished Product and other products of a Party on a percent of sales or other basis consistently applied within and across such Party’s operating units but such allocation is made no less favorable to the Finished Product than to the internal allocation to the Party’s other products.

**“Advertising”** shall mean all costs incurred for the advertising and promotion of Finished Product in the Field and in the U.S. through any means, including, without limitation, (i) television and radio advertisements; (ii) advertisements appearing in journals, newspapers, magazines or other media; (iii) seminars, symposia and conventions; (iv) packaging design; (v) programs for education of professionals (*e.g.*, physicians, practitioners, nurses, pharmacists and other persons with prescription authority); (vi) samples of the Finished Product, visual aids and other selling materials; (vii) hospital formulary committee presentations; (viii) presentations to

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state and other governmental formulary committees, and (ix) all media costs associated with Finished Product advertising as follows: production expense/artwork including set up; design and art work for an advertisement; the cost of securing print space, air time, etc. in newspapers, magazines, trade journals, television, radio, billboards, etc.

**“Trade Promotion”** shall include the allowances given to wholesalers, retailers, brokers, distributors, hospital buying groups, etc. for purchasing, promoting, and distribution of a Finished Product in the Field and in the U.S. This shall include purchasing, advertising, new distribution, and display allowances as well as free goods, wholesale allowances and reasonable field sales samples. To the extent multiple products are involved and some of such products are not Finished Product, then such allowances shall be allocated among the Finished Product and other products of a Party on a percent of sales or other basis consistently applied within and across such Party’s operating units but such allocation is made no less favorable to the Finished Product than to the internal allocation to the Party’s other products.

**“Detailing Costs”** shall include the expenses associated with performing Details. Such expenses shall be calculated on the basis of a fixed rate per PDE (as defined in Article 1) determined by the Finance Subcommittee and approved by the JSC, irrespective of which Party’s Sales Representatives perform the Details.

**“Education”** shall include expenses associated with education of professionals (e.g., physicians, practitioners, etc.) with respect to a Finished Product in the Field and in the U.S. through any means not covered in the definition of “Advertising”, but including articles appearing in journals, newspapers, magazines or other media; seminars, scientific exhibits, and conventions; and symposia, advisory boards and opinion leader development activities; and education grant programs.

#### **4. DISTRIBUTION EXPENSES**

**“Distribution Expenses”** shall be an amount equal to a percentage of Net Sales to be determined after the characteristics and anticipated price of the Finished Product have been determined. Such percentage shall be agreed upon by the Parties in good faith, and shall be designed to approximate Takeda’s cost of distributing such Finished Product in the U.S.

#### **5. CLINICAL PHASE IV AND RELATED EXPENSES**

**“Clinical Phase IV and Related Expenses”** shall include certain costs incurred by a Party in relation to (i) Phase IV Clinical Trials, (ii) product support conducted after the First Commercial Sale of the Product in the U.S., (iii) medical affairs conducted after the First Commercial Sale of the Product in the U.S., and (iv) fees and expenses of outside counsel in respect of regulatory affairs unrelated to obtaining Regulatory Approvals conducted after the First Commercial Sale of the Product in the U.S., all to the extent relating to the Product and not covered by the definitions of the “Marketing Expenses”, “Distribution Expenses” and “Regulatory Expenses”.

## **6. MEDICAL SCIENCE LIAISON EXPENSES**

**“Medical Science Liaison Expenses”** shall include expenses associated with education of medical science liaisons with respect to a Finished Product in the Field and in the U.S., including seminars, scientific exhibits, and conventions; and symposia, advisory boards and opinion leader development activities.

## **7. REGULATORY EXPENSES**

**“Regulatory Expenses”** shall mean all costs incurred after the First Commercial Sale of the Product in the U.S. to maintain all Regulatory Approvals or otherwise incurred in order to comply with all requirements by the Regulatory Authorities, including FDA user and other fees, and costs for reporting, and other regulatory affairs activities, to the extent not covered by the definitions of the “Development Expenses”, “Marketing Expenses”, “Distribution Expenses” and “Clinical Phase IV and Related Expenses”.

## **8. LAUNCH EXPENSE ALLOWANCE**

**“Launch Expenses”** means the Marketing Expenses incurred by either Party on or after the first NDA submission in the U.S. for the Product for the Renal Indication pursuant to the U.S. Commercialization Plan and shared by the Parties in accordance with the last sentence of Section 8.4.

Notwithstanding the foregoing sentence, Takeda shall pay the first \$20,000,000 of Launch Expenses, half of which shall be a loan to Affymax and shall be repaid by Affymax to Takeda in accordance with the following sentence as far as the Product is launched in the U.S. For purposes of repayment to Takeda of such loaned amount, in the calculation of the U.S. Product Profit for each calendar quarter under Section 8.4, Takeda shall be entitled to first deduct and receive 8% of the total Net Sales of the Product in the U.S. in an applicable calendar quarter until such time as Takeda has received \$11,000,000. By way of example, in case the Net Sales in a certain calendar quarter is 100 million Dollars and Commercial Expenses for such calendar quarter is 10 million Dollars (accordingly U.S. Product Profit is 90 million Dollars), then, Takeda is entitled to receive 53 million Dollars among such U.S. Product Profit and Affymax is entitled to receive the remaining 37 million Dollars.

## **9. ALLOCATION OF COSTS OF FINISHED PRODUCT.**

The following guidelines shall be used to allocate costs to the Finished Product in order to calculate the Commercial Expenses:

(a) If the expense is specifically and exclusively used for the Commercialization of a Finished Product in the U.S., 100% of such expense shall be an Commercial Expense.

(b) If the expense is specifically and exclusively used for the Commercialization of a Finished Product (i.e., not for other products of such Party), but both in the U.S. and the Royalty Territory, it shall be allocated 70% to the U.S. and 30% to the Royalty Territory.

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(c) If the expense is not specifically and exclusively used for the Commercialization of a Finished Product (*i.e.*, for other products of such Party), it shall be allocated based on objective means (such as hours spent or amounts consumed) or, if such method cannot reasonably be used, based on a percentage of the sales of each such product or other basis consistently applied within and across such Party's operating units but such allocation is made no less favorable to the Finished Product than to the internal allocation to the Party's other products.

(d) No item of cost shall be duplicated in any of the categories comprising Allowance Expenses.

**EXHIBIT K**  
**INITIAL PRESS RELEASE**



**AFFYMAX AND TAKEDA ANNOUNCE COMPREHENSIVE GLOBAL  
AGREEMENT FOR DEVELOPMENT AND COMMERCIALIZATION  
OF HEMATIDE™ FOR ANEMIA**

***--Companies Will Co-Commercialize with Equal Profit Sharing in the U.S. and Takeda  
Will Commercialize Outside the U.S.--  
--Affymax to Receive \$105 Million Upfront--***

**PALO ALTO, Calif. , and OSAKA, Japan (June 27, 2006)** – Affymax, Inc. (Affymax) and Takeda Pharmaceutical Company Limited (Takeda) today announced that the companies have entered into an exclusive global agreement to develop and commercialize Affymax's lead product candidate, Hematide™, for the treatment of anemia. The companies will collaborate on the development of the product and co-commercialize Hematide™ in the United States while Takeda will hold an exclusive license to develop and commercialize outside the United States, including the right for Japan under the previous agreement announced in February 2006.

Under the terms of the agreement, Affymax will receive US\$105 million in an upfront cash payment. In addition, Affymax is eligible to receive development and regulatory milestone payments of up to US\$280 million, and commercial milestone payments upon successful commercialization of Hematide of up to US\$150 million, for total potential milestone payments of US\$430 million. Takeda and Affymax will be jointly responsible for Hematide U.S. development costs with the vast majority of these costs to be the responsibility of Takeda. Outside of the U.S., Takeda also will be responsible for all of the development costs for regulatory approvals and will pay Affymax royalties on sales. Affymax is responsible for the

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**PATENT**  
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manufacture and supply of drug substance to Takeda, and Takeda is responsible for the final packaging and distribution of Hematide globally.

Hematide, a synthetic, peptide-based erythropoiesis-stimulating agent (ESA), is designed to stimulate the production of red blood cells and is in Phase 2b clinical trials for anemia in dialysis, pre-dialysis and cancer chemotherapy patients. ESAs currently address a US\$12 billion market worldwide and have been used successfully to manage anemia in patients with chronic kidney disease (CKD) and cancer-related anemia. They reduce the need for blood transfusions and the frequency and severity of anemia-associated morbidity, resulting in an improved quality of life for patients.

"Takeda is an ideal global partner because they have the development experience, global commercial capabilities, and financial resources to assist us in our efforts to bring Hematide to market worldwide. Moreover, they have significantly grown their business in the U.S.," said Arlene M. Morris, Affymax's president and chief executive officer. "Takeda has already shown their commitment to Hematide with the rapid filing of an investigational new drug application in Japan and we believe will bring a similar dedication to the development of Hematide globally. We are extremely pleased with this collaboration which we believe will facilitate our efforts to build a fully integrated biopharmaceutical business."

"The opportunity to fully-commercialize Hematide is highly compatible with Takeda's strategy to grow our core therapeutic franchises in cardiovascular disease and diabetes, and oncology," said Yasuchika Hasegawa, Takeda's president. "Many patients with cardiovascular diseases and diabetes suffer from CKD as their underlying disease progresses. Also, Hematide helps address an important need in patients with cancer where anemia is commonly seen in association with chemotherapy or cancer itself. We are very pleased to be able to expand our collaboration with Affymax on such a strategically important product to the worldwide market. We believe that this single-partner collaboration will increase the efficiency of development and accelerate Hematide's commercialization globally."

### **About Affymax**

Affymax, Inc. is a privately-held, clinical-stage pharmaceutical company that is developing a pipeline of synthetic peptide-based drugs against clinically validated targets for the treatment of kidney diseases and cancer. Hematide™, the company's first product candidate to enter the

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clinic, is a novel peptide-based drug designed to stimulate the production of red blood cells. It is in Phase 2 trials for the treatment of anemia associated with chronic kidney disease and cancer. For more information go to [www.affymax.com](http://www.affymax.com).

### **About Takeda**

Takeda, located in Osaka, Japan, is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to striving toward better health for individuals and progress in medicine by developing superior pharmaceutical products. Additional information about Takeda is available through its corporate website, [www.takeda.com](http://www.takeda.com).

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### **For Further Information:**

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## **EXHIBIT L**

[ \* ]

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## EXHIBIT M

### RESOLUTION PROCEDURE FOR DISPUTES AT JSC

1. The Parties shall resolve disputes stipulated in Section 2.5.(c) by final and binding arbitration in accordance with this Exhibit. The Parties shall select a mutually agreeable arbitrator who has significant relevant experience in the subject matter of the disputed issue and no affiliation or pre-existing relationship with either Party. If the Parties cannot agree on an arbitrator within [ \* ] after the senior executive officers have failed to resolve the disagreement, either Party may request the office of the American Arbitration Association located in San Francisco, California to appoint an arbitrator on behalf of the Parties. The date on which such arbitrator is selected shall be the "**Arbitration Commencement Date**."
2. Each Party shall prepare and, within [ \* ] after the Arbitration Commencement Date, deliver to both the arbitrator and the other Party its proposed resolution and a memorandum in support thereof (the "**Support Memorandum**"). The arbitrator shall also be provided with a copy of this Agreement.
3. Within [ \* ] after receipt of the other Party's Support Memorandum, each Party may submit to the arbitrator (with a copy to the other Party) a rebuttal to the other Party's Support Memorandum, which may include a revision, marked to show changes, of either Party's proposed resolution. Neither Party may have communications (either written or oral) with the arbitrator other than for the sole purpose of engaging the arbitrator or as expressly permitted in paragraphs 1 and 2.
4. Within [ \* ] after the receipt of all proposed resolution, Support Memoranda, and rebuttals, if any, the arbitrator shall select from the two proposals provided by the Parties the proposal that the arbitrator believes more accurately reflects the intention of the Parties to this Agreement and the industry customs regarding the manufacture, development and commercialization of comparable pharmaceutical products. The arbitrator's decision shall be provided in writing.
5. The arbitrator shall have reasonable discretion to request additional information, hold a hearing, and extend the time frame for reaching their decision regarding the dispute at issue.
6. The arbitrator's fees and expenses shall be shared equally by the Parties. Each Party shall bear and pay its own expenses incurred in connection with any dispute resolution under this Exhibit M.

## **EXHIBIT N**

[ \* ]

[ \* ]

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## EXHIBIT O

### ROYALTY RATES FOR PRODUCTS [ \* ]

**Royalty Rate.** With respect to any Product that is Developed and Commercialized [ \* ], Takeda shall pay to Affymax royalties based on the aggregate annual Net Sales of the Finished Product sold in the Royalty Territory (including U.S.) at the rate of [ \* ]

All other aspects of the royalty payments (including term, step-downs, credits, etc.) shall be as set forth in Article 8.

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**SCHEDULE 1.9**  
**BACKUP COMPOUNDS**

**Affymax Designation/Description**

[ \* ]

Note: The above-described molecules Controlled by Affymax as of the Effective Date have been

[ \* ]

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## SCHEDULE 10.2

### *Schedule 10.2(b)(i):*

1. [ \* ]

2. On June 9, 2004, Affymax filed a civil complaint in the Regional Court Munich I in the Federal Republic of Germany against Ortho Pharmaceutical Corporation and Ortho-McNeil Pharmaceutical, Inc. of Raritan, New Jersey (collectively "Ortho"). Affymax's complaint alleged that Affymax is an owner of European Patent Application EP 0 892 812 which currently lists Ortho as the sole applicant, and that Affymax should be named as the applicant, or in the alternative as co-applicant, of that European application. [ \* ]. The German case has been dismissed at the request of Affymax and the determination of inventorship and ownership of European Patent Application EP 0 892 812 will be decided by a panel of arbitrators in a binding arbitration under the rules and auspices of the American Arbitration Association; the arbitration is pending with the International Centre for Dispute Resolution captioned as *Affymax v. Ortho-McNeil - AAA Case No. 50 133 T 00165 06*.

3. On September 27, 2004, Affymax filed a civil complaint in the United States District Court for the Northern District of Illinois against Johnson & Johnson, Ortho-McNeil Pharmaceutical, Inc., Ortho Pharmaceutical Corporation, and The R.W. Johnson Pharmaceutical Research Institute d/b/a Johnson & Johnson Pharmaceutical Research and Development (collectively "J&J-Ortho"). Affymax's complaint alleged that J&J-Ortho have applied for and in some cases been granted patents covering subject matter that was invented by Affymax's scientists in connection with a Research and Development Agreement between Affymax and J&J-Ortho ("R&D Agreement"). Affymax alleged that, based on the applicable patent Laws and the R&D Agreement, Affymax's scientists should have been identified as inventors on the patents and patent applications, and Affymax should have been granted ownership rights to these patents and patent applications. The complaint also alleged that J&J-Ortho has breached the R&D Agreement and Affymax has suffered certain damages as a result of said breach. Pursuant to the terms of the R&D Agreement, Affymax entered into a period of good faith discussions with J&J-Ortho to resolve, if possible, the dispute between the parties regarding the subject matter of Affymax's civil complaints in the U.S. and Europe. On October 13, 2004, Affymax and J&J-Ortho entered into a standstill agreement in order to facilitate good faith discussions between the parties to resolve the dispute. On March 8, 2005, Affymax and J&J-Ortho entered into an expanded standstill agreement and Affymax filed a motion to voluntarily dismiss without prejudice the civil complaint in the U.S. District Court in Illinois; the motion was granted and the U.S. complaint was dismissed without prejudice and with leave to refile the complaint with the court prior to September 8, 2005. Affymax filed a Motion to Reinstate the U.S. complaint in the U.S. District Court in Illinois on September 8, 2005, and the motion was granted by the court reinstating the case. On October 10, 2005, Affymax filed an Amended Complaint in the U.S. District Court in Illinois amending the names of the Defendants to reflect the current business units of Ortho and deleting certain claims regarding USSN 60/207,654, USSN 09/863,600 and PCT/US01/16654. On November 1, 2005, Ortho filed an Answer, Affirmative Defenses, and Counterclaims to the Affymax complaint. In their filing, Ortho denies all material claims against

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