Exhibit 1

9-30-85

PRODUCT LICENSE AGREEMENT

THIS PRODUCT LICENSE AGREEMENT entered into this 30th day of September, 1985, by and between AMGEN, a California corporation having offices at 1900 Oak Terrace Lane, Thousand Oaks, California 91320-1789 (said corporation hereinafter referred to as "AMGEN") and ORTHO PHARMACEUTICAL CORPORATION, a New Jersey corporation having offices at U.S. Route 202, Raritan, New Jersey 08869, (said corporation hereinafter referred to as "ORTHO").

WITNESSETH:

WHEREAS, AMGEN represents that it has developed and is continuing to develop technology relating to certain genetically-engineered health-care products and processes for their manufacture;

WHEREAS, AMGEN further represents that it is the owner of patent applications by assignment and unpatented know-how covering said genetically-engineered health-care products;

WHEREAS, ORTHO and AFFILIATES are engaged in the research, development and sale of health care products throughout the world and wish to obtain certain rights to such technology and to such patents and patent applications;

WHEREAS, ORTHO and AMGEN have entered into a TECHNOLOGY LICENSE AGREEMENT on even date herewith for the research, development and regulatory approval of various products;

NOW, THEREFORE, in consideration of the premises and the mutual covenants herein recited, and other good and valuable considerations, the receipt of which is acknowledged, it is agreed as follows:

ARTICLE 1

DEFINITIONS

For the purposes of this Agreement, the terms set forth in this Article I shall have the following meanings:

1.01 "AFFILIATE" shall mean and include (i) any company which owns or controls directly or indirectly at least forty percent (40%) of the voting stock of ORTHO and (ii) any other company at least forty percent (40%) of whose voting stock is owned or controlled directly or indirectly by such owning or controlling company, and (iii) any other company with which

ORTHO or such an owning, owned, controlling or controlled company has a co-marketing, joint venture or distribution agreement for pharmaceuticals outside the United States. The term "ORTHO" shall also mean and include any AFFILIATE wherein the inclusion of same shall be warranted under the provisions of the AGREEMENT.

1.02 "AGREEMENT" shall mean this Product License Agreement.

1.03 "CLOSING" shall occur when,:

(a) AMGEN shall execute and deliver to ORTHO this AGREEMENT and a TECHNOLOGY LICENSE AGREEMENT.

(b) ORTHO shall execute and deliver to AMGEN this AGREEMENT and the TECHNOLOGY LICENSE AGREEMENT; and

(c) The following approvals shall have been obtained: (i) the Executive Committee or the Board of Directors of AMGEN shall have authorized AMGEN's participation in, and its execution and delivery of, this AGREEMENT, including the Exhibits attached hereto and the TECHNOLOGY LICENSE AGREEMENT; and (ii) the Board of Directors of ORTHO shall have authorized ORTHO's participation in, and its execution and delivery of, this AGREEMENT, including the Exhibits attached hereto and the TECHNOLOGY LICENSE AGREEMENT.

1.04 "EFFECTIVE DATE" shall be contingent on certain events and shall mean the date on which this AGREEMENT takes effect which shall be without interruption and simultaneous with the termination of and in accordance with the provisions of Article 9 of the TECHNOLOGY LICENSE AGREEMENT; provided that, if this AGREEMENT takes effect as a result of the receipt of an approval letter to market a LICENSED PRODUCT in a MAJOR COUNTRY or if upon the conclusion of the ten (10) year period there is a pending but as yet unapproved NDA or corresponding registration in any MAJOR COUNTRY, this AGREEMENT shall then be in effect in the entire LICENSED TERRITORY with respect to said PRODUCT. If there is not an approved NDA or corresponding registration in a MAJOR COUNTRY but such approval has been granted to permit marketing of a LICENSED PRODUCT and sales of said LICENSED PRODUCT commence in another country in the TERRITORY, this AGREEMENT shall not come into effect but the payment provisions of Article 4 of this AGREEMENT shall be followed with respect to the sale of LICENSED PRODUCTS in said country.

1.05 "EPO" shall mean erythropoietin as described in Exhibit A.

1.06 "FDA" shall mean the United States Food & Drug Administration and foreign counterparts thereof.

1.07 "GROSS AMOUNT" shall mean NET SALES less all costs related to manufacturing and packaging the LICENSED PRODUCTS into a finished marketable condition.

1.08 "HEPATITIS B" shall mean the recombinant yeast-derived hepatitis B surface antigen vaccine as described in Exhibit B and any other Hepatitis B vaccine development resulting from the Development Program as described in Paragraph 3.01 of the TECHNOLOGY LICENSE AGREEMENT or a supplement of said Program.

1.09 "IL-2" shall mean the recombinant-methionyl human interleukin 2[alanine 125] as described in Exhibit C.

1.10 "LICENSED FIELD" shall mean and include:

(a) with respect to EPO: all indications for human use except dialysis and diagnostics;

(b) with respect to HEPATITIS B and IL-2: all indications for human use except diagnostics.

1.11 "LICENSED KNOW-HOW" shall mean and include any and all data, information, technology or special ability on the part of AMGEN including, but not limited to, processes, techniques, methods, products, materials and compositions relating to the research, development, manufacture, testing

or use of EPO, HEPATITIS B and IL-2, now owned or controlled by AMGEN or that shall be owned or controlled by AMGEN during the term of this AGREEMENT, which is reasonably related to LICENSED PATENTS and LICENSED PRODUCTS for use in the LICENSED FIELD; and which is useful in seeking approval from appropriate governmental health authorities to market LICENSED PRODUCTS and which includes AMGEN's INDs, NDAs and all supplements thereto covering PRODUCTS in the LICENSED FIELD.

1.12 "LICENSED PATENTS" shall mean:

(a) any patent listed in Exhibit D;

(b) any patent application listed in Exhibit D, and any division, continuation, or continuation-in-part of any such application, and any patent which shall issue based on such application, division, continuation or continuation-in-part;

(c) any patent which is a reissue or extension of, or a patent of addition to, any patent defined in (a) or any application maturing into a patent defined in (b) above;

(d) any patent application or patent corresponding to any patent application or patent identified in (a), (b) or (c) above which is hereafter filed or issued in any country; and

(e) any patent application related to or based on any of AMGEN's technical information developed in the LICENSED FIELD during the performance of this AGREEMENT, and any division, continuation or continuation-in-part of any such application; and any patent which shall issue based on such application, division, continuation or continuation-in-part; and any patent which is a reissue or extension of, or a patent of addition to, any such patent.

1.13 "LICENSED PRODUCTS" shall mean and include any PRODUCTS for use in the LICENSED FIELD (i) which are within the scope of a VALID LICENSED CLAIM of a LICENSED PATENT; or (ii) whose use is within the scope of a VALID LICENSED CLAIM of a LICENSED PATENT; or (iii) which are manufactured or packaged within the scope of a VALID LICENSED CLAIM of a LICENSED PATENT; or (iv) which utilize any LICENSED KNOW-HOW.

1.14 "LICENSED TERRITORY" shall mean and include:

(a) with respect to EPO: the United States, its territories and possessions, including the Commonwealth of Puerto Rico;

(b) with respect to HEPATITIS B: the entire world except China;

(c) with respect to IL-2: the entire world.

1.15 "MAJOR COUNTRY' shall mean any of the following: United States, United Kingdom, West Germany, France and Japan.

1.16 "NDA" shall mean a New Drug Application and/or a Product License Application and all supplements filed pursuant to the requirements of the FDA, including all documents, data and other information concerning LICENSED PRODUCTS which are necessary for, or included in, FDA approval to market LICENSED PRODUCTS and foreign counterparts thereof of NDAs.

1.17 "NET SALES" shall mean the amount billed by ORTHO, or an AFFILIATE from the sale of LICENSED PRODUCTS to independent third parties less: (i) discounts, including cash discounts, or rebates actually allowed or granted from the billed amount, (ii) credits or allowances actually granted upon claims or returns regardless of the party requesting the return, (iii) freight charges paid for delivery, and (iv) taxes or other government charges levied on or measured by the billing amount whether absorbed by the billing or the billed party. In the event that LICENSED PRODUCTS are sold in the form of a combination product containing one or more active ingredients, other than EPO, HEPATITIS B or IL-2, NET SALES for such combination products will be calculated by multiplying actual NET SALES of such

LICENSED PRODUCTS by the fraction A/(A+B) where A is the invoice price of the LICENSED PRODUCT if sold separately and B is the total invoice price of any other active component or components in the combination if sold separately by ORTHO or a single AFFILIATE. If on a country-by-country basis the LICENSED PRODUCT and the other active component or components in the combination are not sold separately in said country by ORTHO or a single AFFILIATE, NET SALES for purposes of determining royalties on the combination shall be calculated by multiplying NET SALES of the combination by the fraction C/(C+D) where C is ORTHO's or AFFILIATE's total actual cost of LICENSED PRODUCT at the point of formulation into the combination product and D is ORTHO's or AFFILIATE's total actual cost of the other active ingredient(s) included in the combination product at such point.

1.18 "OUTSIDE RESEARCH PAYMENTS" shall mean amounts paid under the TECHNOLOGY LICENSE AGREEMENT or this AGREEMENT for clinical testing by ORTHO to an individual or individuals or to an entity other than AMGEN, ORTHO or an AFFILIATE for purposes of independent evaluation of any of the PRODUCTS, which data shall be used by ORTHO and/or AMGEN in filing NDAs or other registrations regarding the PRODUCTS.

1.19 "NET PRE-TAX AMOUNT" shall mean the GROSS AMOUNT less all current operating expenses (which operating expenses shall not include manufacturing and packaging as deducted in GROSS AMOUNT nor costs recovered by ORTHO under Paragraphs 4.01 A (iii), 4.01 B (iii) and 4.01 C (iii) of this AGREEMENT) but before income taxes. Any recovery under Paragraphs 4.01 A (iii), 4.01 B (iii) and 4.01 C (iii) by ORTHO shall be made from the GROSS AMOUNTS separate from operating expenses but before determining NET PRE-TAX AMOUNT.

1.20 "PRODUCT ORGANISMS" shall mean any and all organisms developed or acquired by AMGEN, the uses of which are licensed to ORTHO pursuant to this AGREEMENT and which have been genetically engineered to produce biologically active LICENSED PRODUCTS, including any and all improvements thereon.

1.21 "PRODUCTS" shall mean IL-2, HEPATITIS B, and EPO for all human uses in the LICENSED FIELD. Wherever a reference is made to the "PRODUCT" or to the "PRODUCTS", the reference shall apply to each of IL-2, HEPATITIS B and EPO severally, unless the context shall indicate otherwise. Whenever the provisions of this AGREEMENT differ in application to any of IL-2, HEPATITIS B or EPO, then such product shall be identified separately, rather than being referred to as a "PRODUCT".

1.22 "TECHNOLOGY LICENSE AGREEMENT" shall mean an agreement between AMGEN and ORTHO executed on even date herewith.

1.23 "VALID LICENSED CLAIM" shall mean and include a claim in an issued LICENSED PATENT which has not lapsed or become abandoned and which claim has not been declared invalid by an unreversed or unappealable decision or judgment of a court of competent jurisdiction.

ARTICLE 2

LICENSE

2.01 GRANT

(a) AMGEN hereby grants to ORTHO but not AFFILIATES, except as hereinafter provided, an exclusive license to make in one location, have made and use LICENSED KNOW-HOW, LICENSED PATENTS and LICENSED PRODUCTS in the LICENSED TERRITORY in the LICENSED FIELD and to sell LICENSED PRODUCTS in the LICENSED TERRITORY.

(b) AMGEN, having received the consent of Kirin Brewery Co., Ltd., hereby grants to ORTHO but not AFFILIATES, an exclusive license, except as against AMGEN's rights under this AGREEMENT in the LICENSED TERRITORY, to make EPO in one location in the United States for use and sale outside the LICENSED TERRITORY

but not including China and Japan. AMGEN shall provide to ORTHO all information and any assistance and know-how required for ORTHO to achieve the purposes of this paragraph at the earlier of the demonstration of Clinical Efficacy of EPO as defined in the TECHNOLOGY LICENSE AGREEMENT or the completion of PHASE II studies as set forth in an agreement between ORTHO and KIRIN-AMGEN designated "Technology License Agreement" dated September 30, 1985.

2.02 SUBLICENSE

ORTHO may, with prior written notice to AMGEN, sublicense LICENSED PATENTS, LICENSED KNOW-HOW and LICENSED PRODUCTS under this AGREEMENT (i) to any AFFILIATE, or any third party, to use and sell LICENSED PRODUCTS as provided in this AGREEMENT; and (ii) to any one controlled AFFILIATE to make in one location, use and sell LICENSED PRODUCTS as provided in this AGREEMENT. If ORTHO requests the right to sublicense one additional AFFILIATE to make in one location, use and sell LICENSED PRODUCTS as provided in this AGREEMENT, AMGEN shall not unreasonably withhold its consent thereto.

2.03 ASSURANCE BY ORTHO

In the event of sublicensing as provided in Paragraph 2.02, ORTHO shall assure AMGEN that this AGREEMENT shall apply to such AFFILIATE or third party sublicensee, and

such AFFILIATE or third party sublicensee shall deliver to AMGEN a written promise to comply with the terms of this AGREEMENT to the extent that such terms are applicable. ORTHO shall guarantee the due and punctual performance of any and all responsibilities under this AGREEMENT as applied to such AFFILIATE or third party sublicensee.

2.04 DIRECT AGREEMENT

As a substitute for a sublicense, AMGEN shall, if ORTHO so requests, enter into a separate agreement with any AFFILIATE granting a license in accordance with the provisions of this AGREEMENT. Such agreement shall incorporate all of the terms of this AGREEMENT to the extent that they are applicable. ORTHO shall guarantee the due and punctual performance of any and all responsibilities by the AFFILIATE under such separate agreement.

2.05 WARRANTY

AMGEN warrants and represents that it has the full right and power to grant the license set forth in Paragraph 2.01 of this Article 2 and that there are no outstanding agreements, assignments or encumbrances in existence inconsistent with the provisions of this AGREEMENT including, without limitation as to generality, any obligations to governmental agencies or private foundations resulting from acceptance of research grant monies, or otherwise.

2.06 ORTHO EFFORTS

ORTHO agrees to use reasonable efforts to market and sell LICENSED PRODUCTS in the LICENSED TERRITORY.

2.07 IMPROVEMENTS

2.07.1 If AMGEN, on the one hand, or ORTHO and/or its AFFILIATES and sublicensee(s), on the other hand, improve the PRODUCT ORGANISMS, and/or the LICENSED KNOW-HOW, or make LICENSED PRODUCTS or process improvements, all such improvements shall become part of the LICENSED KNOW-HOW and shall be promptly transferred and/or communicated to the other party in order to maintain parity among AMGEN, ORTHO and its AFFILIATES and sublicensees and by the provisions hereof shall be deemed to be a part of the LICENSED PATENTS or LICENSED KNOW-HOW as the case may be and licensed to AMGEN or ORTHO, as the case may be, on a royalty-free basis.

2.07.2 Notwithstanding any provision of this AGREEMENT, any technology and/or improvements developed by a party to this AGREEMENT and disclosed or licensed under this Article 2, shall be and remain the property of the developing party. This Paragraph 2.07.2 shall survive any termination of this AGREEMENT.

patent applications listed in Exhibit D and shall keep ORTHO informed of the status of their prosecution, including such Patent Office proceedings as interferences, reexamination, oppositions and requests for patent term extension under the Act. Notwithstanding the above, AMGEN shall have sole responsibility for all decisions in connection with the filing and prosecution of all patent applications and the maintenance of all patents. AMGEN shall take all appropriate actions to maximize the benefits for both AMGEN and ORTHO with respect to any patent term restoration and/or regulatory exclusivity that may be available in connection with any LICENSED PATENT or LICENSED PRODUCT.

ARTICLE 8

ENFORCEMENT

8.01 INFRINGEMENT BY ORTHO

(i) If, as a result of the manufacture, use and sale of LICENSED PRODUCTS, ORTHO is sued for patent infringement or threatened with such a lawsuit or other action by a third party, then ORTHO shall actively consult with AMGEN in its attempts to resolve same. If the settlement of a lawsuit or threatened lawsuit or other action requires any payments to a third party, then ORTHO and AMGEN shall share said payments on an equal basis.

(ii) If, as a result of the manufacture, use and sale of any LICENSED PRODUCT, ORTHO is sued for patent infringement or threatened with such a lawsuit or other action and as a result of same ORTHO is prevented from the commencement of marketing said LICENSED PRODUCT, then provided that one or more other LICENSED PRODUCTS are being marketed or in the future are marketed or said LICENSED PRODUCT is being marketed in another country or in the future is marketed, ORTHO shall be entitled to recover the following in the manner provided in Paragraph 4.01 hereof from the sale of any LICENSED PRODUCT:

(a) the equivalent of up to 100% of the research and development payments made by ORTHO to AMGEN under Paragraph 3.02 of the TECHNOLOGY LICENSE AGREEMENT for said LICENSED PRODUCT; and

(b) the equivalent of up to 50% of the OUTSIDE RESEARCH PAYMENTS directly related to the LICENSED PRODUCT incurred by ORTHO in accordance with ARTICLE 4 of the TECHNOLOGY LICENSE AGREEMENT

(iii) If, as a result of the manufacture, use and sale of any LICENSED PRODUCT, ORTHO is sued for patent infringement or threatened with such a lawsuit or other action in any country, and as a result of same, ORTHO is prevented from further marketing said PRODUCT in said country then if

(A) said PRODUCT has been on sale less than three (3) years in said country and provided that one or more other LICENSED PRODUCTS are being marketed in any country or in the future are marketed or said LICENSED PRODUCT is being marketed in another country or in the future is marketed, ORTHO shall be entitled to recover the following in the manner provided in Paragraph 4.01 hereof from the sale of any LICENSED PRODUCTS:

(a) the equivalent of up to 100% of the research and development payments made by ORTHO to AMGEN under paragraph 3.02 of the TECHNOLOGY LICENSE AGREEMENT and this AGREEMENT for said LICENSED PRODUCT; and

(b) the equivalent of up to 50% of the OUTSIDE RESEARCH PAYMENTS directly related to the LICENSED PRODUCT incurred by ORTHO in accordance with ARTICLE 4 of the TECHNOLOGY LICENSE AGREEMENT and this AGREEMENT.

(B) said PRODUCT has been on sale more than three (3) years in said country, there shall be no recovery by ORTHO under this Paragraph 8.01 from AMGEN.

(iv) In connection with any lawsuit or threatened lawsuit or other action as set forth in (i), (ii) or (iii) above, ORTHO and AMGEN shall share on an equal basis all reasonable expenses (including attorneys' fees) incurred therewith.

8.02 INFRINGEMENT BY THIRD PARTIES

Either party shall promptly notify the other party of any infringement of any LICENSED PATENTS; misappropriation of a trade secret or declaration of an interference proceeding relating to LICENSED PATENTS or LICENSED KNOW-HOW, and shall provide the other party with all available evidence relating thereto. AMGEN and ORTHO shall then consult with each other as to the best manner in which to proceed. AMGEN shall have the right, but not the obligation, to bring, defend and maintain any appropriate suit or action. If AMGEN requests ORTHO to join AMGEN in such suit or action and ORTHO agrees to do so, ORTHO shall execute all papers and perform such other acts as may be reasonably required and may, at its option, be represented by counsel of its choice. AMGEN shall pay ORTHO its reasonable expenses (including its attorney's fees) in connection with any such suit or action. Should AMGEN lack standing to bring any such action, then AMGEN may cause ORTHO to do so upon first undertaking to indemnify and hold ORTHO harmless (to the extent permissible by law) from all consequent liability and to promptly reimburse all reasonable expense (including attorney fees) stemming therefrom. In the event AMGEN fails to take action with respect to such matters within a reasonable period, not more than six (6) months, following receipt of such notice and evidence, ORTHO shall have the right, but not the obligation, to bring, defend and maintain any appropriatesuit or action. If ORTHO finds it necessary to join AMGEN in such suit or action, AMGEN shall execute all papers and

perform such other acts as may be reasonably required and may, at its option, be represented by counsel of its choice. ORTHO shall pay to AMGEN the reasonable expenses of AMGEN (including its attorney's fees) in connection with any such suit or action. Absent an agreement between the parties to jointly bring any action or suit hereunder and share the expenses thereof, any amount recovered in any such action or suit shall be retained by the party bearing its expenses thereof.

ARTICLE 9

TERM AND TERMINATION

9.01 TERM

This AGREEMENT shall come into effect on the EFFECTIVE DATE and shall remain in effect unless the parties mutually agree in writing to terminate, or until termination occurs pursuant to paragraph 9.02 below.

9.02 DEFAULT

In the event that AMGEN or ORTHO (the "Defaulting party") shall:

a) default in a material obligation hereunder, including failure to make any payments, and fail to remedy such default within 60 days after notice of such default by the Non-Defaulting party; or

EXHIBIT A

DESCRIPTION OF ERYTHROPOIETIN

The chemical structure of r-HuEPO is best described by its amino acid sequence which is depicted below:

NH_2 - ala pro pro arg leu ile cys asp ser arg val leu glu arg try

leu leu glu ala lys glu ala glu Y* asn ile thr thr gly cys ala

glu his cys ser leu asn glu Y asn ile thr val pro asp thr lys

val asn phe tyr ala trp lys arg met glu val gly gln gln ala

val glu val trp gln gly leu ala leu leu ser glu ala val leu

arg gly gln ala leu leu val Y asn ser ser gln pro trp glu pro

leu gln leu his val asp lys ala val ser gly leu arg ser leu

thr thr leu leu arg ala leu gly ala gln lys glu ala ile ser

pro pro asp ala ala ser ala ala pro leu arg thr ile thr ala

asp thr phe arg lys leu phe arg val tyr ser asn phe leu arg

gly lys leu lys leu tyr thr gly glu ala cys arg thr gly asp

arg - COOH

* 'Y' designates N-linked glycosalation site.

Exhibit D-1

ERYTHROPOIETIN

Docket No.	Inventor(s)	Title	Country	S.N.	Filing Date
155	F. Lin	Recombinant Methods and Materials Applied to Microbial Expression of Erythropoietin	U.S.	561,024	12/13/83
155-CIP-1	F. Lin	Recombinant Methods and Materials Applied to Microbial Expression of Erythropoietin	U.S.	582,185	2/21/84
155-CIP-2	F. Lin	Recombinant Methods and Materials Applied to Microbial Expression of Erythropoietin	U.S.	655,841	9/28/84
155-CIP-3	F. Lin	Production of Erythropoietin	U.S.	675,298	11/30/84
132	J. Egrie	ATCC HB8209 - Its Monoclonal Antibody to Erythropoietin ATCC HB8209/Budapest	U.S.	463,724	2/4/83
190	P. Lai T. Strickland	Protein Purification	U.S.	747,119	6/20/85

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