

**Non-Exclusive Sub-License Agreement**  
**For Class I Products, Class II Products, DNA Engineering**  
**In Plants, Transgenics, Viral Engineering**

Between

**Gene Bridges GmbH**, Im Neuenheimer Feld 584, 69120 Heidelberg, Germany

(hereinafter "**GENE BRIDGES**")

and

...

(hereinafter "**LICENSEE**")

the following is agreed upon:

**PREAMBLE:**

Whereas, the European Molecular Biology Enterprise Management Technology Transfer GmbH (hereinafter "**EMBLEM**"), a fully-owned subsidiary of the European Molecular Biology Laboratory (hereinafter "**EMBL**"), is the exclusive licensee of certain U.S. and foreign patents and patent applications owned by EMBL.

Whereas, GENE BRIDGES represents and warrants that EMBLEM granted GENE BRIDGES licenses under particular patents and patent applications with the right to grant sub-licenses.

Whereas, GENE BRIDGES granted an exclusive sub-license to a third party under specific parts of the rights granted by EMBLEM (hereinafter "**Third Party License Agreement**") but retained the right to use, exploit and sublicense these rights within a particular scope.

Whereas LICENSEE desires to sublicense from GENE BRIDGES particular patent rights.

Now, in consideration of the promises and conditions contained herein, GENE BRIDGES and LICENSEE agree to the following:

## **ARTICLE 1**

### **DEFINITIONS**

#### **1.1 Affiliate** shall mean:

Any Person directly or indirectly owned by, owning, or under common ownership with, to the extent 50% or greater, LICENSEE. The term “ownership” shall relate to equity interest (or an equivalent interest), partnership interest (or an equivalent interest), or voting interests.

#### **1.2 Cell** shall mean:

Any cell, including eukaryotic or prokaryotic, whether present individually, or in a group of cells, such as cell lines and tissue.

#### **1.3 Class I Product** shall mean:

A DNA construct which is, or is intended to be, used to alter a mammalian cell so that said mammalian cell (i) carries a genetic modification resulting from the insertion of the said DNA construct targeted to a predetermined, specific chromosomal location without the intent to alter the function or expression of the gene(s) at the site of the targeted chromosomal location; and (ii) is or is intended to be used to create a line of mammalian animals (the “**Class I Animals**”). For clarity, Class I Product includes the said DNA construct (the “**Class I Construct**”), the said altered mammalian cell (the “**Class I Cell**”) and the said altered mammalian animal line. Class I Product only includes the insertion of DNA sequences that are not intended to (a) alter the function or expression of the gene(s) at the site of the targeted chromosomal location, or (b) have a phenotypic impact on the said altered mammalian animal line. Examples of DNA sequences which can be inserted in ways that would not alter the function or expression of the gene(s) at the site of the targeted chromosomal location and thus would be expected not to have a phenotypic impact, are those encoding reporter proteins such as GFP or lacZ, cell surface markers, protein tags or trans-acting utility proteins, such as recombinases including

Cre and FLP recombinases, but do not include libraries of cDNAs to be screened for phenotypic effects of their misexpression. For clarity, a Class I product is commonly known as “conditional knock-out”, “reporter strain”, “cell-surface marker”, “protein tagging”, “transacting utility protein” (such as Cre, Flp, or Fre Recombinase).

**1.4 Class II Product** shall mean:

A DNA construct which is used to, or is intended to, alter a mammalian cell so that said mammalian cell (i) carries a genetic modification resulting from the insertion of the said DNA construct targeted to a predetermined, specific chromosomal location with the intent to alter the function or expression of the gene(s) that was at, or is inserted into, the site of the targeted chromosomal location; and (ii) is or is intended to be used to create a line of mammalian animals (the “**Class II Animals**”). For clarity, Class II Product includes the said DNA construct (the “**Class II Construct**”), the said altered mammalian cell (the “**Class II Cell**”) and the said altered mammalian animal cell line. Class II Product includes DNA constructs designed to delete all or part of a gene sequence or replace all or part of a gene sequence with a reporter, such as LacZ or GFP, as well as gain-of-function Class II Products whereby a DNA sequence is inserted into a predetermined, specific chromosomal location in a mammalian cell with the intention to test the phenotypic impact of the inserted DNA sequences on the said altered mammalian animal line. For examples, gain-of-function Class II Products include the insertion beside a chosen gene of another gene, the insertion of a dominant negative allele of a chosen gene, the insertion of a cDNA, or the insertion of any other gene with the intent to examine its phenotypic impact in the said altered mammalian animal line. For clarity, a Class II Product is commonly known as “receptor modification”, “gain-of-function of a specific gene”, “conventional knock-out” and “conventional knock-in”.

**1.5 Commercial** shall mean:

An action or service for a Third Party in exchange for financial benefits or any other consideration including but not limited to an acquisition of shares or rights or an exchange of materials or information.

**1.6 Diagnostic Procedure** shall mean:

A procedure related to the detection of chosen DNA or RNA sequences.

**1.7 Effective Date** shall mean:

The date of the last party's signature hereof.

**1.8 In-House Research Purposes** shall mean:

The non-Commercial use of the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method (Licensed Technology) in the research facilities of the LICENSEE or its Affiliates, solely for the research purpose of the LICENSEE. For clarity, Research Purposes do not include the making of any product which can be sold or transferred or is made with these objectives.

**1.9 Know-how** shall mean:

All information, know-how, experiences, or trade secrets pertaining to the use of the Licensed Technology provided by GENE BRIDGES to LICENSEE, including but not limited to the specific information indicated in **Annex I**.

**1.10 Licensed Technology** shall mean:

Methods for generating Class I Constructs, Class II Constructs, Transgenic Constructs, Viral Engineering Constructs, Transgenic Plant Constructs or modifications of bacterial chromosomes using the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method covered by the Patent Rights listed in **Annex II**

**1.11 Mammalian Construct** shall mean:

A DNA construct allowing genetic modification of a mammalian Cell and/or a mammalian Organism.

**1.12 Metabolic Engineering** shall mean:

Cloning, shuffling and/or modification, in particular through cloning, subcloning, deletion, insertion and/or mutation, of genes, gene fragments or nucleic acids containing those genes whose products are involved in the synthesis pathways of secondary metabolites, in particular in the polyketide, non-ribosomal peptide synthase and fatty acid synthase pathways (the "**Metabolic Genes**").

**1.13 Organism** shall mean:

The complete organism and/or part(s) thereof.

**1.14 Patent Rights** shall mean:

The rights of GENE BRIDGES in patents and patent applications PCT-Application WO 99/29837 claiming priority of the European Patent Application No. 97 121 462.2 (December 5, 1997) and 98 118 756.0 (October 5, 1998), which issued January 2003 as US patent No. 6,509,156 - and the PCT-Application WO 01/04288 claiming priority of U.S. Application no. 09/350,830 (filed July 9, 1999), which issued March 12, 2002, as US patent 6,355,412. A list of these patent applications and corresponding national patent applications is attached as **Annex II**. "Patent Rights" shall include any continuations, continuations-in-part, divisionals, foreign counterparts, and issued patents based thereon.

**1.15 Person** shall mean:

Any natural person, corporation, general partnership, limited partnership, joint venture, proprietorship, organization, university, academic or research institution, or other business or not-for-profit entity.

**1.16 Recombinant Service** shall mean:

A service provided by LICENSEE to its Affiliates or any Third Party, in which LICENSEE is provided financial benefits or any other consideration including but not limited to an acquisition of shares or rights or an exchange of materials or information in exchange for the alteration, generation, cloning or subcloning of any nucleic acid.

**1.17 Red<sup>®</sup>/ET<sup>®</sup> Recombination Method** shall mean:

A recombination method for specific modification of bacterial chromosomes or *E. coli* compatible DNA target molecules, by *in vivo* homologous recombination with a targeting DNA molecule in prokaryotic cells. The position at which the target molecules are modified is determined by the design of the targeting molecule with which the target molecule recombines. The method also encompasses direct cloning and subcloning of target DNA sequences from various donor molecules. The method is described and claimed in further detail in the Patent Rights.

**1.18 Research Product** shall mean:

Any nucleic acid generated and/or modified using the Red<sup>®</sup>/ET<sup>®</sup> Recombinant Method and any DNA, RNA, nucleic acid fragment, and vector that contains the same or is derived therefrom, whether purified or in a mixture (including libraries) or in a living, quiescent or dead Cell or Organism as well as proteins encoded by aforementioned nucleic acids as covered by the Patent Rights. For clarity, a Research Product that is also a Class I, Class II, Transgenic, Transgenic Plant or Viral Engineering Construct within the definitions given herein is not considered a Research Product with respect to the license granted under Article 2.

**1.19 Third Party** shall mean:

A Person other than LICENSEE, GENE BRIDGES or any of their respective Affiliates.

**1.20 Transgenic** shall mean:

A DNA construct which is, or is intended to be, used to alter a mammalian cell so that said mammalian cell carries a genetic modification resulting from the insertion of the said DNA construct that is not targeted to a predetermined, specific chromosomal location, with or without the intent to alter the function or expression of the gene(s) at the site of the chromosomal insertion. Said DNA construct may be used to create a line of mammalian animals (the “**Transgenic Animals**”). For clarity, Transgenic includes the said DNA construct (the “**Transgenic Construct**”), the said altered mammalian cell (the “**Transgenic Cell**”) and the said altered mammalian animal line. Transgenic does not include Class I or Class II Products.

**1.21 Transgenic Plant** shall mean:

A DNA construct which is, or is intended to be, used to alter a plant cell, so that said plant cell carries a genetic modification resulting from the insertion of the said DNA construct. Said DNA construct may be used to create a line of plants (the “**Transgenic Plant**”). For clarity, Transgenic Plant include the said DNA construct (the “**Transgenic Plant Construct**”), the said altered plant cell (the “**Transgenic Plant Cell**”) and the said altered plant.

**1.22 Viral Engineering Product** shall mean:

A DNA construct, which is used to clone, shuffle or modify DNA or pieces of DNA that are partially or completely leading, or are meant to lead to, the *in vivo* or *in vitro* production of a virus regardless of the replication competence or incompetence of said virus (the “**Viral**

**Engineering Construct**". Virus includes all viruses whose life cycle is dependent upon either single-stranded or double-stranded DNA or RNA. Said DNA construct may be used to create cell lines (the "**Viral Engineering Cell Line**") or a virus (the "**Modified Virus**"), however, Viral Engineering Constructs which are also a Class I or II Constructs within the definitions given herein are not considered Viral Engineering Constructs with respect to the license granted under Article 2.

**1.23 Year** shall mean:

The twelve-month calendar year starting on 1<sup>st</sup> January and ending on 31<sup>st</sup> December.

## ARTICLE 2

### SUBLICENSE GRANT

#### 2.1 Non-exclusive License for Class II Products - Sublicense Limit

Subject to the terms and conditions of this Agreement, GENE BRIDGES hereby grants LICENSEE a worldwide, non-exclusive sublicense under the Licensed Technology to make up to 25 Class II Products per Year in its production facilities (but not the facilities of any other Third Party - "**The Sublicense Limit**") and to use said Class II Products. The license granted comprises the right of LICENSEE to sell, have sold, offer for sale, import, or use for resale, export, and/or otherwise distribute Class II Cells and Class II Animals, but not Class II Constructs, whereby the Sublicense Limit applies accordingly for the distribution etc. of these Class II Cells and Class II Animals. Further details of the Sublicense Limit are provided in Section 2.11.

#### 2.2 Non-exclusive License for Class I Products

GENE BRIDGES hereby grants LICENSEE a worldwide, non-exclusive license under the Licensed Technology to make and use Class I Products. The license granted to LICENSEE comprises the right to sell, have sold, offer for sale, import or use for resale, export and/or otherwise distribute Class I Cells and Class I Animals, but not Class I Constructs. There is no

Sublicense Limit for Class I Products, i.e. Class I Products can be made, etc. as provided above in an indefinite number.

### **2.3 Non-exclusive License for Transgenics**

GENE BRIDGES hereby grants to LICENSEE a worldwide, non-exclusive, license under the Licensed Technology to make and use Transgenics. The license granted to LICENSEE comprises the right to sell, have sold, offer for sale, import or use for resale, export and/or otherwise distribute Transgenic Cells and Transgenic Animals, but not Transgenic Constructs. There is no Sublicense Limit for Transgenics, i.e. Transgenics can be made, etc. as provided above in an indefinite number.

### **2.4 Non-exclusive License for Transgenic Plants**

GENE BRIDGES hereby grants to LICENSEE a worldwide, non-exclusive, license under the Licensed Technology to make and use Transgenic Plants. The license granted to LICENSEE comprises the right to sell, have sold, offer for sale, import or use for resale, export and/or otherwise distribute Transgenic Plant Cells and Transgenic Plants, but not Transgenic Plant Constructs. There is no Sublicense Limit for Transgenic Plants, i.e. Transgenic Plants can be made, etc. as provided above in an indefinite number.

### **2.5 Non-exclusive License for Viral Engineering Products**

GENE BRIDGES hereby grants to LICENSEE a worldwide, non-exclusive, license under the Licensed Technology to make and use Viral Engineering Products. The license granted to LICENSEE comprises the right to sell, have sold, offer for sale or resale export and/or otherwise distribute Viral Engineering Cell Lines, Modified Viruses but not Viral Engineering Constructs. There is no Sublicense Limit for Viral Engineering Products, i.e. Viral Engineering Products can be made, etc. as provided above in an indefinite number.

### **2.7 Non-exclusive Research License for In-House Research Purposes**

GENE BRIDGES hereby grants LICENSEE a worldwide, non-exclusive, non-transferable sublicense to use the Red<sup>®</sup>/ET<sup>®</sup> Recombinant Method for In-House Research Purposes. For clarity, this does not include the right to sell, have sold, offer for sale or resale export and/or otherwise distribute Research Products.



## **2.8 No Allowance for Sublicense Grant**

LICENSEE is not entitled to grant any sublicense in the right(s) granted by GENE BRIDGES according to Sections 2.1, 2.2, 2.3, 2.4, 2.5, 2.6 or 2.7 to transfer or assign these licensed right(s). In case of a sale of LICENSEE, wherein at least 50% of the equity interest (or an equivalent interest), partnership interest (or an equivalent interest), or voting interests in LICENSEE are sold to a Third Party, or in case of a merger of LICENSEE with a Third Party, this Agreement is automatically terminated ("auflösende Bedingung" - resolutive condition). In this case, no remuneration or repayment of the license fees paid by LICENSEE (cf. Article 3) will occur. GENE BRIDGES is prepared to negotiate a new license with said Third Party and resulting company, respectively, in good faith.

## **2.9 Diagnostic Procedure, Recombinant Service, Metabolic Engineering**

LICENSEE is in particular not entitled to the following uses of the Red/ET Recombination Method:

2.8.1 Use in a Diagnostic Procedure

2.8.2 Use in a Recombinant Service

2.8.3 Use in Metabolic Engineering. For clarity, the generation of Class I, II Transgenic, Transgenic Plant or Viral Engineering Constructs containing and/or targeting Metabolic Genes is considered Metabolic Engineering.

## **2.10 Field of Use Limitation**

The parties acknowledge that they are, within this Article 2, defining the field of use of the Patent Rights by the constructs, cells and animals that can be made, used, sold, etc. per Year. For purposes of determining the number of Class II Products referred to in Section 2.1, all DNA constructs, cells or animals carrying the identical genetic alteration shall be counted as one (1) Class II Product. LICENSEE shall use the date of manufacture of the DNA construct for purposes of determining the number of Class II Products that have been made per Year. Any DNA construct that can be shown to have failed to result in a cell with the desired modification shall not be counted as part of the total number of allowed Class II Products, provided that LICENSEE documents such failures by completing the form attached hereto as **Annex III** for

each such failure. The completed forms must be delivered to GENE BRIDGES and will be treated confidential.

#### **2.11a Class II Product Limit [for a LICENSEE in the U.S.]**

According to the rights retained in Third Party License Agreement, GENE BRIDGES is entitled to supply LICENSEE with a specific amount of Class II Products. This amount – the “**Class II Product Limit**” – is 25 per Year in the United States (including Puerto Rico, the “U.S.”). The number of Class II Products made by LICENSEE pursuant to Section 2.1 is deducted from the Class II Products Limit, i.e. the 25 Class II Products that can be purchased per Year from GENE BRIDGES.

#### **2.11b Class II Product Limit [for a LICENSEE outside the U.S.]**

According to the rights retained in Third Party License Agreement, GENE BRIDGES is entitled to supply LICENSEE with a specific amount of Class II Products. This amount – the “**Class II Product Limit**” – is 75 per Year.

#### **2.11c Sublicense Limit [for a LICENSEE in the US]**

If LICENSEE purchases Class II Products from GENE BRIDGES or imports Class II Products into the U.S., the number of Class II Products purchased or imported per Year is deducted from the Sublicense Limit, i.e. the 25 Class II Products that can be made by LICENSEE per Year pursuant to Section 2.1. Example: LICENSEE purchases 10 Class II Products in a given Year from GENE BRIDGES, then LICENSEE has the right to make up to 15 Class II Products in the same Year. LICENSEE shall use the date of receipt of the Class II Products for purposes of determining the number of Class II Products that have been purchased from GENE BRIDGES.

#### **2.11d Export Limit into the U.S.[for a LICENSEE outside the U.S.]**

LICENSEES making and/or purchasing Class II Products are not entitled to export or cause the exportation of more than 25 Class II Products per Year into the U.S.

#### **2.12 Execution of a Certificate**

If the LICENSEE makes Class II Products with the Licensed Technology, the LICENSEE will execute a certificate attached hereto as Annex IV or Annex V at the end of each Year and deliver it to GENE BRIDGES no later than January 31<sup>st</sup> of the following year.

### ARTICLE 3

#### FINANCIAL CONSIDERATION

##### 3.1 Initial payment / Sign on Fee

There is an initial payment of Euro Five Thousand (5000) excluding VAT tax due within thirty (30) days of the Effective Date of this Agreement. Payments shall be made to GENE BRIDGES. A delay in payment in excess of thirty (30) days after the Effective Date will result in an additional surcharge of 2% of the total payment due per calendar month. Should the license fee payment be delayed by more than two (2) months after the Effective Date, GENE BRIDGES shall have the right to terminate this non-exclusive license agreement.

##### 3.2 Annual Sub-License Fee and Renewal

An annual sub-license fee of Euro .....(see table of license fees) excluding VAT tax is due on the first and each following Effective Date of the respective Year. This sub-license fee is calculated with regard to LICENSEE staff levels and according to the table of licensee fees, at the time of signing. Significant changes in the LICENSEE's staff levels at the date of renewal can result in an increase in the annual renewal fee. The annual renewal fee will also be adjusted to accommodate the annual inflation rate (at a maximum of 3% annually).

A delay in payment in excess of thirty (30) days after the Effective Date will result in an additional surcharge of 2% of the total payment due per calendar month. Should the license fee payment be delayed by more than two (2) months after the Effective Date, GENE BRIDGES shall have the right to terminate this non-exclusive license agreement.

##### 3.3a Excess of the Sublicense Limit or Class II Product Limit [for a LICENSEE in the US]

An additional sub-license fee of US\$ 100,000 per Class II Product in excess of the Sublicense Limit shall be payable to GENE BRIDGES immediately following any Year in which LICENSEE (including its Affiliates) makes more than the Sublicense Limit. GENE BRIDGES shall have the right to assign its rights against LICENSEE to a Third Party for purposes of enforcing GENE BRIDGES' rights to claim the license fee and damages. The same applies if the Class II Product Limit is exceeded, in case that LICENSEE is supplied by GENE BRIDGES with Class II Products. Thus, for clarity, said additional license fee per excess Class II Product becomes payable immediately following any Year in which LICENSEE (including its Affiliates) makes and/or receives from GENE BRIDGES and/or imports into the U.S (in any combination) more than a **total** of 25 Class II Products.

### **3.3b Excess of the Sublicense Limit or Class II Product Limit [for a LICENSEE outside US]**

An additional sub-license fee of US\$ 100,000 per Class II Product in excess of the Sublicense Limit shall be payable to GENE BRIDGES immediately following any Year in which LICENSEE (including its Affiliates) makes more than the Sublicense Limit. GENE BRIDGES shall have the right to assign its rights against LICENSEE to a Third Party for purposes of enforcing GENE BRIDGES' rights to claim the license fee and damages. The same applies if the Class II Product Limit is exceeded, in case that LICENSEE is supplied by GENE BRIDGES with Class II Products. Thus, for clarity, said additional license fee per excess Class II Product becomes payable immediately following any Year in which LICENSEE (including its Affiliates) makes and/or imports into the U.S (in any combination) more than a **total** of 25 Class II Products and/or receives from GENE BRIDGES more than a **total** of 75 Class II Products.

### **3.4 Taxes / Distribution costs**

All turnover taxes and indirect taxes (i.e. VAT) shall be borne by LICENSEE. All distribution costs for items and documents which must be provided by GENE BRIDGES shall be borne by LICENSEE. The Party required to deduct withholding taxes shall do so and promptly pay such tax. Each Party agrees to assist the other Party, as may reasonably be necessary, in claiming exemption from or reduction of such deduction or withholding under a double taxation treaty.

The Parties also agree to assist each other by providing documentation as is needed to claim a repayment of or a credit for the withholding tax.

## **ARTICLE 4**

### **IMPROVEMENTS**

#### **4.1 Modifications of Licensed Technology**

LICENSEE is allowed to further develop the Licensed Technology. LICENSEE shall report all improvements or modifications of the Licensed Technology to GENE BRIDGES. LICENSEE shall disclose any such improvements or modifications of the Licensed Technology to GENE BRIDGES in writing within sixty (60) days after its actual or constructive reduction to practice.

#### **4.2 Joint Inventions**

Any and all intellectual property rights including, without limitation, patent rights and Know-How and improvements generated by LICENSEE and GENE BRIDGES jointly in the course of or as a result of this Agreement shall belong to LICENSEE and GENE BRIDGES jointly depending on the respective inventive contribution.

#### **4.3 Improvements of GENE BRIDGES**

GENE BRIDGES shall retain full rights to the Licensed Technology (including all intellectual property rights thereunder), and any improvements and modifications to the Licensed Technology that might be created exclusively by GENE BRIDGES.

#### **4.4 Improvements by LICENSEE**

Patentable improvements of the Licensed Technology made solely by LICENSEE shall belong to LICENSEE alone. However, in consideration for the rights granted hereunder LICENSEE shall grant to GENE BRIDGES, an irrevocable, worldwide, royalty-free, non-exclusive license with the right to sub-license for all patentable derivatives of Materials, any other patentable reagents, methods or improvements related to the Licensed Technology and the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method.

**ARTICLE 5**  
**CONFIDENTIALITY**

**5.1** Except as expressly contemplated by the license granted hereunder, LICENSEE shall not disclose or transfer, sell, distribute and/or exchange to any Third Party any confidential or secret information or trade secrets confided or made available by GENE BRIDGES (collectively “**Confidential Information**”) in particular, (1) data or information of any kind, including Know-how, as well as (2) Material.

This obligation of confidentiality does not apply to Confidential Information which:

- (a) was known and can be proven by documentary evidence to be known to LICENSEE prior to disclosure by GENE BRIDGES; or
- (b) is or becomes, through no fault of LICENSEE, accessible to the public, the burden of proof lies with the LICENSEE; or
- (c) can be shown by LICENSEE to have been obtained from a third party entitled to disclose such information; or
- (d) is the subject of a written permission to disclose provided by GENE BRIDGES.

**5.2** LICENSEE may disclose Confidential Information pursuant to an order of a competent court or administrative agency, provided that it has informed GENE BRIDGES of such order, and has used reasonable efforts to limit the scope of the disclosure and to obtain confidential treatment by the court or administrative agency of the Confidential Information disclosed pursuant to such order.

**5.3** This obligation of confidentiality shall survive expiration and/or termination of this Agreement or any part of it for a period of five (5) years from the time of disclosure of such Confidential Information. The obligations of confidentiality apply to LICENSEE.

**5.4** LICENSEE will cause employees that use the Licensed Technology or that have knowledge of Know-how to be under non-disclosure obligations with respect thereto that are at least as restrictive as those prescribed in **Annex VI**.

## ARTICLE 6

### USE OF THE NAMES EMBL; EMBLEM; GENE BRIDGES AND LICENSEE

LICENSEE may not use the name EMBL or EMBLEM for any purpose. In any promotional materials developed and/or used by LICENSEE concerning any products made using the Licensed Technology, the name GENE BRIDGES may be included as

“From the inventors of the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method”

LICENSEE agrees that it shall provide GENE BRIDGES with an opportunity to review and comment on all such promotional materials that include the name GENE BRIDGES. LICENSEE agrees to incorporate all changes reasonably requested by GENE BRIDGES.

LICENSEE agrees that GENE BRIDGES is entitled to publicly announce and list LICENSEE among its customers, if LICENSEE obtains products produced by the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method from GENE BRIDGES, and among the users of the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method, respectively, provided, however, that GENE BRIDGES is not entitled to describe the terms of this agreement or the nature of the Services in such listing.

## ARTICLE 7

### WARRANTIES AND INDEMNITIES

**7.1** GENE BRIDGES does not assume liability for any damage occurring through the use of the Licensed Technology for any purpose, in particular arising out of the care, handling, disposal or transfer, unless the claim is due to the intentional misconduct or gross negligence of GENE BRIDGES. GENE BRIDGES gives no warranty nor makes any representation, express or implied, with regards to the suitability of the Licensed Technology for any applications or purposes of LICENSEE.

**7.2** GENE BRIDGES warrants that to the best of its knowledge, it has been authorized by EMBLEM to sub-license the Licensed Technology as provided for herein. Additionally, GENE BRIDGES warrants that the rights retained within the Third Party License Agreement comprise and cover the right granted to LICENSEE, i.e. the right of LICENSEE with regard to Class II Products as provided by Section 2.1.

**7.3** GENE BRIDGES represents and warrants as follows:

- (a) this Agreement is and shall be a legal and valid obligation binding upon GENE BRIDGES, enforceable in accordance with its terms;
- (b) the execution and delivery of this Agreement, does not and will not constitute a breach or violation of any other agreement or understanding, written or oral, to which it is a party; and
- (c) the execution, delivery and performance of this Agreement have been duly authorized by all necessary corporate action on the part of GENE BRIDGES, and the person executing this Agreement on behalf of GENE BRIDGES has been duly authorized to do so by all requisite corporate action.

**7.4** LICENSEE represents and warrants as follows:

- (a) this Agreement is and shall be a legal and valid obligation binding upon LICENSEE, enforceable in accordance with its terms;
- (b) the execution and delivery of this Agreement, and the use of the Licensed Technology, do not and will not constitute a breach or violation of any other agreement or understanding, written or oral, to which it is a party;
- (c) the execution, delivery and performance of this Agreement have been duly authorized by all necessary corporate action on the part of LICENSEE, and the person executing this Agreement on behalf of LICENSEE has been duly authorized to do so by all requisite corporate action; and
- (d) LICENSEE shall use the Licensed Technology in accordance with all applicable laws, rules and regulations.

**7.5** GENE BRIDGES guarantees neither the patentability nor the validity of the Patent Rights, and shall not be liable accordingly.

**7.6** LICENSEE guarantees that it has not previously made use of the Licensed Technology, or will not in future make use of the Licensed Technology, without a valid a Sub-License Agreement to use the Licensed Technology, from GENE BRIDGES.



**ARTICLE 8**  
**NO-CHALLENGE CLAUSE**

LICENSEE agrees not to challenge the patentability or validity of the Patent Rights during the duration of the license Agreement and not to support, directly or indirectly, third parties in challenging the patentability or validity of the Patent Rights.

**ARTICLE 9**  
**PARTIAL OR COMPLETE LACK OF PATENTABILITY OR**  
**INVALIDITY OF PATENT RIGHTS**

**9.1 Lack of Patentability; Invalidity of the Patent Rights**

This Agreement and its validity shall not be influenced by the fact that the Patent Rights should be finally declared not patentable or invalid. LICENSEE shall, however, have the right to terminate this agreement within three months from such final declaration for the last patent, if this declaration has effect for all regions that the license was granted for.

**9.2 No Remuneration of Payments and License Fee**

Previously made payments as set out in Section 3 or payments made in advance shall be non-refundable. Annual Renewal payments that were due prior to the final rejection of the Patent Rights or the final declaration of invalidity, but have not yet been paid, have to be paid by the LICENSEE.

**ARTICLE 10**  
**TERM AND TERMINATION**

**10.1 Duration**

This Agreement shall be entered into for the duration of one (1) Year. It is extended Year by Year for one Year unless it is terminated by written notice three (3) months prior to each Effective by one of the parties.

### **10.2 Material Breach**

In the event of a material breach or default in the performance of this Agreement by either party which is not cured within sixty (60) days after the receipt of written notice thereof from the other party, the party not in breach or default shall be entitled without prejudice to any of its other rights to terminate this Agreement by giving written notice to take effect immediately upon receipt. In particular, it is understood and agreed by the parties that any use by LICENSEE of the Licensed Technology outside the scope of the license grant set forth in Section 2.1, in particular non-compliance with the Sublicense Limit, in Section 2.9, 2.10 - 2.11 and/or the lack of execution of the certificate set forth in Section 2.13 shall be considered a "material" breach or default in the performance of this Agreement resulting in GENE BRIDGES' right to terminate this Agreement immediately upon written notice to LICENSEE.

### **10.3 EMBLEM Agreement**

GENE BRIDGES is entitled to terminate the Agreement with immediate effect, if the license granted by EMBLEM with regard to the Patent Rights has been terminated or revoked by EMBLEM.

### **10.4 Expiration of the Patent Rights**

In any case, this Agreement shall terminate upon the expiration of the last-to-expire of the patents issued on the Patent Rights.

### **10.5 Effect of Termination**

Upon termination of this Agreement (except as provided by Sections 9.1 and 10.4), LICENSEE will immediately cease to use the Licensed Technology and shall issue to Gene Bridges a written statement within thirty (30) days of the date of termination that the LICENSEE has ceased to use the License Technology and will not use the Licensed Technology again without a new sub-license to the Licensed Technology from Gene Bridges.

For clarification, LICENSEE is under no obligation to cease using the Licensed Technology should this Agreement be terminated pursuant to Section 9.1 or Section 10.4.

## **ARTICLE 11**

### **GENERAL CONDITIONS**

#### **11.1 Amendments and Modifications**

Amendments and modifications to this Agreement including the amendment and modification of this provision may be made only in writing signed by both parties.

#### **11.2 Governing Law; Jurisdiction**

This Agreement shall be governed by and construed in accordance with the substantive laws of the Federal Republic of Germany, without reference to conflicts of law principles. The parties hereby unconditionally submit to the exclusive jurisdiction of the District Court Mannheim, Germany.

#### **11.3 Assignment**

This Agreement may be assigned by GENE BRIDGES or its successors in interest, assigns, trustees and other legal representatives.

#### **11.4 Waiver**

Any failure by a party to insist upon strict performance of any provision hereof, at anytime or for any period of time, shall not constitute a waiver of, or estoppel against asserting, the right to require such performance in the future. No waiver of any term or condition of this Agreement shall be effective unless set forth in a written instrument duly executed by or on behalf of the party waiving such term or condition.

### 11.5 Force Majeure

Neither party shall be liable or deemed to be in breach of this agreement by reason of any delay in performing, or failure to perform, any of its obligations if the delay or failure was due to any cause beyond that party's control. Causes beyond a party's reasonable control include, but are not limited to, an act of God, explosion, flood, tempest, fire or accident, war or threat of war, sabotage, insurrection, civil disturbance or requisition, acts, restrictions, bye-laws, prohibitions, or measures of any kind on the part of any governmental, parliamentary or local authority, import or export regulations or embargoes, strikes, lock-outs or other industrial actions or trade disputes (whether involving employees of Gene Bridges, customer or a third party), difficulties in obtaining raw materials, materials from suppliers, labor, fuel parts or machinery, power failure, power surge or spike, telecommunications failure or breakdown of machinery.

### 11.6 Successors and Assigns

This Agreement shall be binding upon, and inure to the benefit of, the parties, successors and permitted assigns.

### 11.7 Annexes

All Annexes are part of this Agreement.

LICENSEE:

GENE BRIDGES :

Name

Signature

Gary Stevens  
Name

Title

Chief Executive Officer  
Title

\_\_\_\_\_  
Date

\_\_\_\_\_  
Date

## **Annex I**

### **Know How**

- 1) Instruction and/or trouble-shooting guides and manuals
- 2) Training materials
- 3) Protocols
- 4) Any information, such as advice, strategy consultation, technical details, protocols, references and other know-how reduced to writing by GENE BRIDGES within twenty-one (21) days after it has been furnished by GENE BRIDGES and/or its affiliates to the LICENSEE

will be included in this provision. A copy of such information reduced to writing will be sent to the LICENSEE

Workshops and training programs at GENE BRIDGES' or at any of its affiliate(s) facilities or at the facilities of the LICENSEE can be arranged for and will be charged for separately.

#### Attachments:

Copies of the information indicated above

## Annex II

### Patent Rights

- I. Patent Application PCT/EP98/07945, Novel DNA Cloning Method (ET) Priority date December 5, 1997;
- II. U.S. Patent Application no. 09/350,830 filed July 9, 1999, Directed Cloning and Subcloning;
- III. Related know how and reagents complementary to the patent and patent applications listed in Exhibit B; and
- IV. US Patent nos. 6,355,412 and 6,509,156B by Stewart et.al. including the following related patents and applications:

<b>US 6509156 FAMILY</b>			
<b>Country</b>	<b>Title</b>	<b>Appln. No.</b>	<b>Filing Date</b>
Austria	Neue Methode Zur Klonierung Dns Unter Anwendung Des E. Coli Rece/Rect Rekombinationssysteme	AT19980963541T	12/07/98
Australia	Novel DNA Cloning Method	AU19990018771	12/07/98
Australia	Novel DNA Cloning Method	AU19990018771D	12/07/98
Canada	Novel DNA Cloning Method	CA19982312474	12/07/98
Germany	DNA Cloning Method Relying On The E. Coli Rece/Rect Recombination System	DE19986015384	12/07/98
Germany	DNA Cloning Method Relying On The E. Coli Rece/Rect Recombination System	DE19986015384T	12/07/98
Denmark	DNA Cloning Method Relying On The E. Coli Rece/Rect Recombination System	DK19980963541T	12/07/98
Europe	Novel DNA Cloning Method Relying On The E. Coli Rece/Rect Recombination System	EP19980963541	12/07/98
Europe	Novel DNA Cloning Method Relying On The E. Coli RECE/RECT Recombination System	EP20020021915	12/07/98
Spain	DNA Cloning Method Relying On The E. Coli Rece/Rect Recombination System	ES19980963541T	12/07/98
Japan	DNA Cloning Method Relying On The E. Coli RecE/RecT Recombination System	JP20000524410T	12/07/98
Portugal	Novo Metodo De Clonagem De Adn Baseado No Sistema De Recombinacao Rece/Rect De E. Coli	PT19980963541T	12/07/98

<b>US 6509156 FAMILY</b>			
<b>Country</b>	<b>Title</b>	<b>Appln. No.</b>	<b>Filing Date</b>
United States	DNA Cloning Method Relying On The E. Coli Rece/Rect Recombination System	US20000555510	06/05/00
United States	Novel DNA Cloning Method	US20020231013	08/30/02
United States	Novel DNA cloning method	US20040842534	05/11/04
PCT	Novel DNA Cloning Method	WO1998EP07945	12/07/98

<b>US 6355412 FAMILY</b>			
<b>Country</b>	<b>Title</b>	<b>Appln No.</b>	<b>Filing Date</b>
Australia	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	AU20000066911	07/10/00
Australia	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	AU20000066911D	07/10/00
Brazil*	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	BR20000012283	07/10/00
Canada	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	CA20002377938	07/10/00
China	Method And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	CN20000812739	07/10/00
Europe	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	EP20000954461	07/10/00
Israel	No English Title Available	IL147385D	Unavailable
Japan	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	JP20010509492T	07/10/00
Mexico	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	MX2002PA00233	07/10/00
Poland	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	PL20000353634	07/10/00
United States	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	US19990350830	07/09/99
PCT	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	WO2000EP06533	07/10/00
South Africa	Methods And Compositions For Directed Cloning And Subcloning Using Homologous Recombination	ZA20020000152	01/08/02





## Annex III

CONFIDENTIAL – FOR INTERNAL USE ONLY

CERTIFICATION OF ABANDONMENT OF A CONSTRUCT DUE TO FAILURE TO GENERATE A CELL

[COMPANY NAME]

1. Brief description of the construct: \_\_\_\_\_

2. Graphic representation of the construct:



3. Method used to determine failure to generate a cell (e.g. Southern blot, PCR, etc.):

\_\_\_\_\_

I certify the construct described above has been destroyed.

\_\_\_\_\_  
Representative

\_\_\_\_\_  
Date:

## Annex IV (US-License)

[INSERT DATE]

Gene Bridges GmbH  
Im Neuenheimer Feld 584  
D-69120 Heidelberg, Germany

To Whom it May Concern:

[YOUR NAME] (“Company”) hereby certifies to Gene Bridges GmbH (“Gene Bridges”) that it, together with its Affiliates (as defined below), has not made under its sublicense more than 25 Class II Products (as defined below), less any Class II Products purchased or received from Gene Bridges during the YEAR [INSERT YEAR] and has not purchased or received from Gene Bridges more than 25 Class II Products, less any Class II Products made under its sublicense, i.e. has not purchased or received from Gene Bridges or made more than 25 Class II Products per Year in total.

Class II Products shall mean: A DNA construct which is, or is intended to be, used to alter a mammalian cell so that said mammalian cell (i) carries a genetic modification resulting from the insertion of the said DNA construct targeted to a predetermined, specific chromosomal location with the intent to alter the function or expression of the gene(s) that was at, or is inserted into, the site of the targeted chromosomal location; and (ii) is, or is intended to be, used to create a line of mammalian animals. For clarity, Class II Product includes the said DNA construct, the said altered mammalian cell and the said altered mammalian animal cell line. Class II Products include DNA constructs designed to delete all or part of a gene sequence or replace all or part of a gene sequence with a reporter, such as LacZ or GFP, as well as gain-of-function Class II Products whereby a DNA sequence is inserted into a predetermined, specific chromosomal location in a mammalian cell with the intention to test the phenotypic impact of the inserted DNA sequences on the said altered mammalian animal line. For examples, gain-of-function Class II Products include the insertion beside a chosen gene of another gene, the insertion of a dominant negative allele of a chosen gene, the insertion of a cDNA, or the insertion of any other gene with the intent to examine its phenotypic impact in the said altered mammalian animal line.

AFFILIATE shall mean: Any entity directly or indirectly owned by, owning, or under common ownership with, to the extent 50% or greater, Company.

The term "ownership" shall relate to equity interest (or an equivalent interest), partnership interest (or an equivalent interest), or voting interest.

For purposes of determining the number of Class II Products referred to above, all DNA constructs, cells or animals carrying the identical genetic alteration shall be counted as one (1) Class II Product. Company shall use the date of manufacture of the DNA construct or the date of receipt of the Class II Constructs, cells or animals from Gene Bridges, as the case may be, for purposes of determining the number of Class II Products that are made, purchased or received per Year. Any DNA construct that can be shown to have failed to result in a cell with the desired modification shall not be counted as part of the total number of allowed Class II Products.

YEAR shall mean: the twelve-month calendar year starting on 1<sup>st</sup> January and ending on 31<sup>st</sup> December.

Sincerely,

[YOUR NAME]

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## Annex V (non-US License)

[INSERT DATE]

Gene Bridges GmbH  
Im Neuenheimer Feld 584  
D-69120 Heidelberg, Germany

To Whom it May Concern:

[YOUR NAME] (“Company”) hereby certifies to Gene Bridges GmbH (“Gene Bridges”) that it, together with its AFFILIATES (as defined below), has not made under its sublicense more than 25 Class II Products (as defined below) and has not received and/or purchased more than 75 Class II Products during the YEAR [INSERT YEAR]. Furthermore, Company certifies that it has not exported (or caused the exportation of) more than 25 Class II Products either supplied by Gene Bridges or made under the sublicense to the United States (including Puerto Rico) during the YEAR [INSERT YEAR].

Class II Products shall mean: A DNA construct which is, or is intended to be, used to alter a mammalian cell so that said mammalian cell (i) carries a genetic modification resulting from the insertion of the said DNA construct targeted to a predetermined, specific chromosomal location with the intent to alter the function or expression of the gene(s) that was at, or is inserted into, the site of the targeted chromosomal location; and (ii) is, or is intended to be, used to create a line of mammalian animals. For clarity, Class II Product includes the said DNA construct, the said altered mammalian cell and the said altered mammalian animal cell line. Class II Products include DNA constructs designed to delete all or part of a gene sequence or replace all or part of a gene sequence with a reporter, such as LacZ or GFP, as well as gain-of-function Class II Products whereby a DNA sequence is inserted into a predetermined, specific chromosomal location in a mammalian cell with the intention to test the phenotypic impact of the inserted DNA sequences on the said altered mammalian animal line. For examples, gain-of-function Class II Products include the insertion beside a chosen gene of another gene, the insertion of a dominant negative allele of a chosen gene, the insertion of a cDNA, or the insertion of any other gene with the intent to examine its phenotypic impact in the said altered mammalian animal line.

AFFILIATE shall mean: Any entity directly or indirectly owned by, owning, or under common ownership with, to the extent 50% or greater, Company

The term “ownership” shall relate to equity interest (or an equivalent interest), partnership interest (or an equivalent interest), or voting interest.

For purposes of determining the number of Class II Products referred to above, all DNA constructs, cells or animals carrying the identical genetic alteration shall be counted as one (1) Class II Product. Company shall use the date of manufacture of the DNA construct or the date of receipt of the Class II Constructs, cells or animals from Gene Bridges, as the case may be, for purposes of determining the number of Class II Products that are made, purchased or received per Year. Any DNA construct that can be shown to have failed to result in a cell with the desired modification shall not be counted as part of the total number of allowed Class II Products.

YEAR shall mean: the twelve-month calendar year starting on 1<sup>st</sup> January and ending on 31<sup>st</sup> December.

Sincerely,

[YOUR NAME]

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## Annex VI

### Secrecy Obligation

The undersigned ..... herewith undertakes to keep secret and not to disclose to any third party and/or not to use or exploit on its own account or for a third party any information and know-how related to and required for performing the Red<sup>®</sup>/ET<sup>®</sup> Recombination Method and not to transfer DNA constructs, cell lines and bacterial strains with which the Red/ET Recombination Method can be enhanced, facilitated or performed, which has been or will be made available or accessible to him by ... [name of employer] or GENE BRIDGES GmbH, Dresden, or affiliates of GENE BRIDGES.

"Red/ET Recombination Method " in this context is a recombination method that allows site-specific modification of E. coli compatible DNA target molecules by in vivo homologous recombination with a linear DNA molecule using the Red/ET cloning mechanism. The Red/ET Recombination Method is subject to patent protection.

This secrecy obligation prevails during the duration of the employment relationship and after its termination, provided that the information or know-how is and remains secret, i.e. unknown in the public domain.

\_\_\_\_\_  
Place and Date

\_\_\_\_\_  
Signature