

CLINICAL RESEARCH AGREEMENT

PROTOCOL NUMBER RNA003142-302

THIS AGREEMENT, when signed by both parties, will set forth certain agreements by and between PharmaNet, LLC, having its principal place of business at 504 Carnegie Center, Princeton, New Jersey ("PharmaNet") and San Mateo Medical Center ("Institution") having a place of business at 222 W. 39th Avenue, San Mateo, California.

WHEREAS, PharmaNet is acting as an independent contractor of Ribapharm Inc. ("Sponsor") to arrange and administer a multicenter study (the "Study") to clinically evaluate Sponsor's drug, Viramidine ("Study Drug"), and has entered into an agreement with Sponsor concerning the design, funding, and administration of such a Study;

WHEREAS, Joanne Imperial, M.D. is employed by Institution and shall serve as Principal Investigator ("Investigator") for this Study in accordance with Sponsor's Study protocol no. RNA003142-302 (the "Protocol") as more specifically defined below in Article 1;

WHEREAS, Investigator has reviewed sufficient information regarding the Study Drug and the Protocol for the proposed clinical Study to evaluate his or her interest in participating in the proposed Study and desires to participate as an Investigator in the Study;

NOW, THEREFORE, the parties, in consideration of the mutual covenants and promises contained herein, have entered into this Agreement (the "Agreement") and do specifically agree as follows:

1. **Study Protocol.** The scope and nature of the Study entitled "A Randomized, Double-Blind, Multicenter Study to Compare the Safety and Efficacy of Viramidine to Ribavirin in Treatment-Naïve Patients with Chronic Hepatitis C", will be conducted in strict accordance with the Protocol attached hereto as Appendix I, and any approved amendments thereto. The Protocol fully details the respective clinical research activities and responsibilities to be undertaken, pursued, and followed with all due diligence, by the Institution and Investigator. The Protocol will be considered final after it is signed by the Sponsor and Investigator and approved by the pertinent Institutional Review Board (IRB). Thereafter, the Protocol may be amended only by prior written consent of Sponsor and subsequent approval by the IRB (collectively, the Protocol and approved amendments shall be referred to herein as the "Study"). A copy of the signed Investigator's statement referred to in Article 2, Conduct of Study, below and Protocol amendments will be maintained in the Institution's Study files.

2. **Conduct of Study.** Institution represents that it and the Investigator have the experience, capabilities, adequate subject population and resources, including but not

limited to sufficient personnel and equipment, to accurately, efficiently and expeditiously perform the Study in a professional and competent manner.

Institution agrees to administer and Investigator agrees to conduct this Study in strict compliance with any and all applicable federal, state, and local laws, regulations, good clinical practices, all requirements of the Institution, and any other relevant professional standards, and specifically to conduct the Study in accordance with the Statement of Investigator, FDA Form 1572, as described in 21 CFR §312.53, which Investigator has completed, signed, and delivered to PharmaNet prior to the commencement of the Study at the site. To the extent terms and conditions in this Agreement and the Protocol conflict, the terms and conditions of the Protocol shall control. The Institution and Investigator further agree that in the performance of the Study the Institution, its employees and agents, and the Investigator and the research staff shall devote their best efforts to accurately and efficiently perform the work required under this Agreement, which efforts shall include but are not limited to:

- a. Investigator's exercise of independent medical judgment as to the compatibility of each patient with Protocol requirements;
- b. Obtain from each patient in the Study a signed consent form in accordance with the Protocol which has been approved by the IRB, PharmaNet, and Sponsor in accordance with 21 CFR §56, et. sec., or any successor thereto;
- c. Properly perform and direct or administer the Study in accordance with the Protocol, the requirements of 21 CFR §312.50, et. sec., Subpart D, entitled, "Responsibilities of Sponsors and Investigators," the FDA's published guideline entitled, "Good Clinical Practices, Consolidated Guideline", and the other requirements as set forth herein. Notwithstanding the foregoing, if in the course of performing this Agreement, generally accepted standards of clinical research and medical practice relating to the benefit, well-being and safety of any subject requires a deviation from the Protocol, such standards will be followed. In such case, the party aware of the need for a deviation shall immediately notify PharmaNet and Sponsor of the facts supporting such deviation as soon as the facts are known to said party. This notification shall be followed by written notification of the same;
- d. Review all patient case report forms (hereinafter "CRFs") to assure their accuracy and completeness, and assist PharmaNet's and Sponsors' representatives and clinical monitors upon request in promptly resolving any discrepancies or errors on CRFs and in performing random audits of original patient records, laboratory reports, or other raw data sources underlying data recorded on the CRFs;
- e. Submit all data and information, and undertake all activities, so that the time schedules set forth in the Protocol and this Agreement are strictly met;
- f. Notify Sponsor, PharmaNet and the IRB by facsimile or electronic transmission immediately upon knowledge, and in no event later than the time periods

specified by the regulations and the IRB, of any unanticipated or serious adverse reactions to the Study Drug or control drug;

Date: 27 May 2004
Investigator: Joanne Imperial, M.D.

- g. Maintain records of patient identification, clinical observations, laboratory tests, and drug receipt, storage, return and disposition as specified in the Protocol;
- h. Provide all reasonable cooperation with PharmaNet and Sponsor in all of their efforts to monitor the Study; and
- i. Represent and affirm that neither Investigator nor Institution, nor to its knowledge any of the individuals performing the Study is under investigation by the FDA for debarment action or is presently debarred pursuant to the Generic Drug Enforcement Act of 1992 (21 U.S.C. 301 et seq), and notify PharmaNet immediately upon any inquiry concerning or the commencement of any such proceeding concerning any such person.
- j. Pursuant to 21 CFR §312.66, assure that the IRB will comply with the requirements of 21 CFR §56, et. sec.

3. **Replacement** In addition to any other remedy which may be available to PharmaNet, in the event Investigator becomes either unwilling or unable to perform the duties required by this Agreement, upon request by PharmaNet, Institution will cooperate, in good faith and expeditiously, to find a replacement Investigator acceptable to PharmaNet and Sponsor. Institution's and Investigator's cooperation in finding an acceptable replacement does not negate their obligations to perform this Agreement up to effective date of replacement.

4. **Term and Termination** The term of this Agreement shall begin upon its execution by both parties hereto and shall continue until the objectives of the Study are accomplished unless sooner terminated as as provided herein.

- a. PharmaNet reserves the right to discontinue work to be performed by the Institution and Investigator and to cancel this Agreement without cause upon thirty (30) days written notice to Institution and Investigator.
- b. This Agreement may be terminated by PharmaNet effective immediately for any of the following reasons:
 - (1) Authorization and approval to conduct the Study is withdrawn by the United States Food and Drug Administration;
 - (2) PharmaNet determines in its discretion that the emergence of any unexpected or unanticipated significant safety issue with the Study Drug administered in the Study is of such magnitude or incidence in the opinion of either the Institution, Investigator, PharmaNet, and/or Sponsor to support termination;

- (3) PharmaNet determines in its sole discretion that Investigator has failed to recruit or enroll a sufficient number of subjects for participation in the Study to make it likely that the statistical requirements applicable to the Study will be met; or

- (4) Sponsor terminates its clinical research agreement with PharmaNet for conduct of the Study, unless Sponsor otherwise assumes the obligations of PharmaNet hereunder and undertakes to continue with the conduct of the Study.
- c. This Agreement may be terminated by any party upon thirty (30) days written notice of termination for a material breach of this Agreement by the other party and if such breach is not cured within said thirty (30) day period.
- e. Immediately upon receipt of a notice of termination, Investigator shall cease entering subjects into the Study, shall cease conducting procedures to the extent medically permissible on subjects already entered into the investigational Protocol, and shall refrain from incurring additional costs and expenses to the extent possible.
- f. In the event of termination, the sum payable under this Agreement shall be limited to prorated fees based on actual work performed pursuant to the Protocol as determined in accordance with the Budget (as defined below). Any funds not due Institution under this methodology for payment but already paid to Institution shall be returned to PharmaNet within thirty (30) days of the site close-out visit by PharmaNet.

5. **Budget and Payment** In consideration for performance of the Study, PharmaNet will pay Institution in accordance with the Budget and Milestone Payment Schedule attached as Appendix II hereto and made a part hereof (the "Budget"). The Budget may be modified only upon the prior written consent of the parties. Payments shall be made in accordance with the provisions set forth in the Budget, with the last payment being made after PharmaNet has received all completed CRFs, with all queries resolved to the satisfaction of PharmaNet, and, if PharmaNet requests, the return of all other "Confidential Information" as defined in Article 6 and "Sponsor Technology" defined in Article 7.

Investigator acknowledges and agrees that his or her judgment with respect to his or her advice to and care of each patient is not affected by the compensation Institution receives hereunder. [Institution and Investigator acknowledge and agree that they are not entitled to direct payment from Sponsor.]

6. **Confidential Information** For purposes of this Agreement, the term "Confidential Information" shall mean and refer to the Protocol, all Study data, including but not limited to patient records (exclusive of patient medical records), Investigational Drug Brochure, CRFs, laboratory work sheets, slides, reports, materials and all other information, generated as a result of the Study or provided by either the Sponsor or PharmaNet. Such information shall be accurate, complete, and legible, and will be promptly and fully disclosed to and produced for the inspection and use of PharmaNet and Sponsor at any reasonable time upon request. The Institution also agrees to supply

to PharmaNet and Sponsor the pertinent IRB periodic reports, at intervals agreed to by the parties but not to exceed twelve months, on the progress of each Study.

7. **Sponsor Technology** For purposes of this Agreement, the term "Sponsor Technology" shall mean all data, materials, and information, know-how, methods or techniques, whether or not patented or patentable, copyrighted or copyrightable, pertaining to the research, development, manufacture, or use of compounds obtained or developed by, or on behalf of, Sponsor which is disclosed to the Institution for the purpose of assisting the Institution in administering and Investigator in performing the Study. In the performance of this Agreement, PharmaNet or Sponsor may disclose Sponsor Technology to Institution and Investigator. Such Sponsor Technology shall remain the confidential and proprietary property of Sponsor. Institution acknowledges that Sponsor is the sole and exclusive owner of the Sponsor Technology disclosed, whether or not patented or subject to copyright or patent protection; and that the Sponsor Technology is commercially valuable and has not been disclosed publicly.

8. **PharmaNet Property** In addition to the foregoing, Institution and Investigator acknowledge that PharmaNet possesses or may in the future possess certain inventions, processes, know-how, trade secrets, improvements, other intellectual properties and other assets, including but not limited to analytical methods, procedures and techniques, procedure manuals, personnel data, financial information, computer technical expertise and software, which have been independently developed by PharmaNet and which relate to its business or operations (collectively "PharmaNet's Property"). Institution and Investigator agree that any of PharmaNet's Property or improvements thereto which are used, improved, modified or developed by Institution and or Investigator under or during the term of this Agreement are the sole and exclusive property of PharmaNet, except to the extent that such improvements or modifications include, incorporate or are based upon the Sponsor Technology.

9. **Nondisclosure** Institution and Investigator shall maintain in strict confidence all of the Confidential Information, the Sponsor Technology and PharmaNet's Property (each "Non-disclosable Matter" and collectively "Non-disclosable Matters herein), and not disclose or disseminate to any third party or use for any purpose other than the performance of the Study any of the same. Confidential Information and Sponsor Technology shall remain the confidential and proprietary property of Sponsor, and shall be disclosed only on a need-to-know basis and only to the Investigator, the Institution and Institution's employees and agents, or any investigator replacement (individually a "Required Disclosee"), if any, agreed to by Sponsor pursuant to Article 3, Replacement. Institution and/or Investigator will inform and advise each Required Disclosee of the obligations hereunder and each of the Required Disclosee shall be bound by such obligations in a like fashion.

The foregoing obligation of non-disclosure shall not apply to Non-disclosable Matters:

- a. at or after such time that the Non-disclosable Matter is or becomes publicly available through no fault of the Institution or Investigator;

- b. at or after such time that the Non-disclosable Matter is disclosed to Institution of Investigator by a third party legally entitled to disclose such information and not subject to any obligation of confidence;

- c. Any Non-disclosable Matter that is already known to Institution or Investigator prior to disclosure hereunder, as shown by prior written records, provided Institution and/or Investigator so advises PharmaNet and Sponsor within fifteen (15) days after disclosure hereunder;
- d. Non-disclosable Matters necessary to obtain IRB approval of the Study or if Confidential Information must be included in any patient's written informed consent form when disclosed exclusively for those purposes; or
- e. to the extent a Non-disclosable Matter is required by applicable law to be disclosed to federal, state, or local authorities, provided that Institution and Investigator will immediately notify PharmaNet and Sponsor of such request and take reasonable steps to limit the scope of such disclosure.

Institution and Investigator agree to use reasonable best efforts to ensure that each of the individuals rendering services hereunder treat the Non-disclosable Matters as confidential and that such individuals are familiar with the terms of this Agreement relating to confidentiality.

Upon completion of the Study or earlier termination, all Non-disclosable Matters furnished to the Institution and/or Investigator in tangible form shall be returned to the disclosing party, provided however, the Institution may retain one copy of Confidential Information in a secure location for purposes of identifying Institution's obligations hereunder.

10. **Injunctive Relief** Institution and Investigator acknowledge and agree that any violation of the terms of this Agreement relating to the disclosure or use of Confidential Information or Sponsor Technology may result in irreparable injury and damage to Sponsor not adequately compensable in money damages, and for which Sponsor will have no adequate remedy at law. Institution and Investigator acknowledge and agree, therefore, that if those disclosure terms are violated, Sponsor may need to obtain injunctions, orders, or decrees in order to protect the Confidential Information and the Sponsor Technology.

11. **Publication** Institution acknowledges that the Study involves multiple clinical sites, and that the Sponsor reserves the right to first publish or present the combined data of this multiple site study. Thereafter, upon the submission of a multi-center publication or one year after the termination of the Study, whichever occurs first, Institution shall be free to publish the results from patients treated at the Institution. Institution agrees to submit a copy of all proposed publications and/or presentations to Sponsor for its review at least sixty (60) days prior to the estimated date of publication and/or presentation, and if no response is received within sixty (60) days of the date submitted to Sponsor, it will be conclusively presumed that the publication and/or presentation may proceed without delay. If Sponsor determines that the proposed publication and/or presentation contains patentable subject matter which requires protection, Sponsor may require the

delay of publication and/or publication for a period of time not to exceed ninety (90) days for the purpose of filing patent applications.

12. **Release of Information** Sponsor may use, refer to, and disseminate reprints of scientific, medical, and other published articles relating to the Study which disclose the name of Investigator, consistent with U.S. copyright laws. Institution and or Investigator shall not disclose publicly the existence of this Agreement, except to the extent required by academic policies or law. No party to this Agreement shall use the name of any other party hereto or Sponsor in connection with any advertising or promotion of any product or service without the prior written permission of such party or Sponsor, as appropriate.

13. **Independent Contractors** Each party to this Agreement shall act as an independent contractor and shall not be construed for any purpose as the partner, agent, employee, servant, or representative of the other party. Accordingly, the employee(s) of one party shall not be considered to be employee(s) of the other party, and neither party shall enter into any contract or Agreement with a third party which purports to obligate or bind the other party.

14. **Drug Storage and Return** In accordance with 21 CFR §312.59 and upon completion of the Study, all unused compounds, drugs, devices, equipment, and related materials and all copies of Sponsor Technology that were furnished to Investigator shall be returned to PharmaNet upon PharmaNet's request and expense. Regarding all unused compounds and or drugs, the Institution and Investigator shall, upon the direction and approval of PharmaNet, either 1) return all such material back to the Sponsor; 2) destroy such material at the site where the Study is being conducted, in a manner that does not expose humans to risk from the compound or drug; or 3) dispose of such materials in another method that that does not expose humans to risk from the compound or drug. The Investigator shall keep all Study Drugs in a locked, secured area at all times and maintain complete, up-to-date records showing receipt of shipments of the Study Drug, dispensing of the Study Drug and returns of the Study Drug as required by the Protocol, applicable federal, state, and local laws, regulations, and guidelines.

15. **Audits** Investigator shall notify PharmaNet immediately by telephone or facsimile if the U.S. Food and Drug Administration or other duly authorized authority requests permission to or does inspect Investigator's facilities or research records during the term of this Agreement and will, to the extent allowed by law, provide in writing to PharmaNet copies of all materials, correspondence, statements, forms, and records which Investigator receives, obtains or generates pursuant to any such inspection.

During the term of this Agreement, Investigator will permit PharmaNet's representatives to examine or audit the work performed hereunder, the facilities systems and equipment at or with which the work is conducted and records related to such work, upon reasonable advance notice during regular business hours to determine that the project assignment is being conducted in accordance with the agreed requirements and that the facilities are adequate.

16. Patent Rights and Inventions It is expressly agreed that neither Sponsor and or PharmaNet on the one hand, or Institution and/or Investigator on the other, transfers by operation of this Agreement to the other hereto any patent right, copyright or other proprietary right which either party hereto owns as of the commencement of this Agreement, except as specifically set forth herein.

The ownership of any information, inventions, or discoveries (whether patentable, copyrightable, or not), innovations, suggestions, ideas, communications and reports (collectively "Inventions"), conceived, reduced to practice, made or developed by the Institution and/or the Investigator and/or all individuals or entities either employed by or subcontracted by Institution and/or Investigator, as a result of and relating to the conduct of the Study, belong to the Sponsor and will be considered and deemed "work made for hire" for the benefit and exclusive ownership of the Sponsor to the fullest extent permitted by law; provided, however, if any such Works (or portion thereof) shall not be legally qualified as a "work made for hire", or shall subsequently be so held not to be a "work made for hire", then Institution and/or Investigator and/or all individuals or entities either employed by or contracted by Institution and/or Investigator agrees to assign all of their interests therein without compensation to Sponsor or its nominee whenever requested to do so by Sponsor. Institution and/or Investigator and/or all individuals or entities either employed by or contracted by Institution and/or Investigator agrees they will execute any and all applications, assignments, or other instruments and live testimony which Sponsor shall deem necessary to apply for and obtain Letter Patent of the United States or of any foreign country or to otherwise protect the Sponsor's interest therein, and Sponsor shall reimburse Institution and Investigator for their time devoted to said activities.

Further, Institution and/or Investigator will disclose to Sponsor and PharmaNet any and all Inventions conceived, reduced to practice, made or developed by the Institution and/or the Investigator, as a result of conducting their obligations hereunder. However, if the Institution and/or the Investigator obtains ownership of any invention arising from research conducted under the Study, Sponsor shall be granted the first opportunity to acquire an exclusive license for use of the invention based on good faith negotiations between the Institution and/or the Investigator and Sponsor.

17. Insurance, Indemnification and Limitation of Liability.

- a. The following insurance coverages shall be maintained throughout the term of the Study:
 - (1) Sponsor warrants and represents that is has and shall maintain, at its own expense, a policy or program of insurance or self-insurance providing clinical trials coverage at levels not less than \$5,000,000 for each occurrence of bodily injury, personal injury or death.

- (2) Institution warrants and represents that it has and shall maintain, at its own expense, a policy or program of insurance or self-insurance providing comprehensive general liability coverage with limits not less than \$1,000,000 per occurrence and \$3,000,000 in the aggregate, and professional liability coverage with limits not less than \$1,000,000 per occurrence and \$3,000,000 in the aggregate covering each the Institution and the Investigator.
- b. Sponsor shall defend, indemnify and hold the Institution its Investigator, trustees, officers, agents and their respective employees (collectively referred to as the "Institutional Indemnities" herein), harmless from any and all liabilities, claims, actions or suits for personal injury or death, arising out of or in connection with the study drug(s) during the course of the Study for which study drug is supplied or manufactured by Sponsor, provided that:
- (1) The Study is conducted in accordance with the Protocol and all written instructions delivered by Sponsor concerning administration of the Research study drugs or devices under the Study and Good Clinical Practice regulations, and in a manner required of a reasonable and prudent clinical investigator or physician;
 - (2) Such loss does not arise out of the negligence, gross negligence or intentional misconduct or inaction of any Institutional Indemnity; and
 - (3) The Sponsor is notified as soon as practicable of any complaint, claim or injury relating to any loss that is subject to this indemnification.
- c. PharmaNet expressly disclaims any and all liability whatsoever in connection with this Agreement, the Study Drug, [the Protocol] and the conduct and performance by the parties and Sponsor hereunder except with respect to payment of amounts properly payable to Institution pursuant to Article 5 (Budget and Payment) above and, without limiting the foregoing, expressly disclaims any and all liability for or in respect of any product claim arising out of a condition caused by or allegedly caused by the administration of the product being tested. The Institution and/or the Investigator expressly acknowledges and agree that PharmaNet shall have no liability whatsoever to them with respect to such matters, including without limitation any type of damages, whether direct, consequential or otherwise.

18. **Complete Agreement, Amendment** The parties agree that this Agreement constitutes the sole, full, and complete Agreement by and between the parties and supersedes all other written and oral agreements and representations between the parties with respect to the items herein, except where in conflict with the Protocol. No amendments, changes, additions, deletions, or modifications to or of this Agreement

shall be valid unless reduced to writing and signed by the parties. Any requests for changes or amendments or other notices or communications concerning this

Agreement should be in writing or shall be deemed to have been given when mailed by U.S. Mail postage prepaid or bonded courier and forwarded to the following:

To PharmaNet: PharmaNet, LLC
Patricia A. Mosher
Senior Director, Clinical Research
504 Carnegie Center
Princeton, NJ 08540
Phone: (609) 951-6881
Fax: (609) 514-0390

To Institution: San Mateo Medical Center
Anita Booker
Clinical Trials and Research Unit
222 West 39th Avenue
San Mateo, CA 94403

19. **Applicable Law** This Agreement shall be construed, governed, interpreted, and applied in accordance with the laws of the State of New Jersey, exclusive of its conflicts of laws provisions. Venue for any disputes that may arise under this Agreement will be in the State of New Jersey.

[For non-US contracts, substitute the following language: "Any disputes that may arise under this Agreement will be decided by a court of competent jurisdiction."]

20. **Binding Effect** This Agreement shall be binding upon the parties, their legal representatives, successors, and assigns. The obligations of the parties contained in Articles 6 (Confidential Information), 7 (Sponsor Technology), 8 (PharmaNet Property), 9 (Nondisclosure), 10 (Injunctive Relief), 11 (Publication), 12 (Release of Information), 14 (Drug Storage and Return), 16 (Patent Rights & Inventions), and 17 (Limitation of Liability) shall survive the termination or expiration of this Agreement. Sponsor shall be an intended third party beneficiary hereunder and the parties hereto agree that the terms and conditions of this Agreement may be enforced by Sponsor directly against the Institution, the Investigator, and PharmaNet despite any claims or defenses one party may have against the other.

21. **Payee** Institution designates the following party as Payee under this Agreement. Institution acknowledges that it has advised Payee that Payee is accepting tax liability for the work performed under this Agreement. This information needs to be completed below and on the attached IRS Form W-9 and returned to PharmaNet prior to the receipt of ANY Study payment. This information will be used for preparation of Federal Form 1099 which will be issued to each Payee documenting the payments made to the Payee in each calendar year.

Date: 27 May 2004
Investigator: Joanne Imperial, M.D.

IT IS IMPERATIVE THAT THE PAYEE NAME CORRESPONDS TO THE TAX IDENTIFICATION NUMBER LISTED BELOW.

Payee Name: San Mateo Medical Center
Clinical Trials and Research Unit
Pay To Address: 222 West 39th Avenue
San Mateo, CA 94403
Payee's (9-Digit) Tax ID #: 946000532

22. **Waiver** Failure to insist upon compliance with any of the terms and conditions of this Agreement shall not constitute a general waiver or relinquishment of any such terms or conditions, and the same shall remain at all times in full force and effect.

23. **Assignment** It is expressly understood by the parties there to that Institution may not assign, delegate, subcontract or transfer any of its rights or obligations under this Agreement to any party without the express, written consent of PharmaNet.

Upon 10 days notice to Institution, PharmaNet may assign any or all of its rights or obligations under this Agreement without the consent of Institution.

24. **Effective Upon Execution; Authority** This Agreement shall not be considered accepted, approved, or otherwise effective until signed below by the appropriate parties. Each of the parties hereto represents and warrants that the person signing below on such party's behalf has the authority to enter into this Agreement, and that this Agreement does not violate any existing agreement or obligation of such party. The Institution and Investigator and further acknowledges and agrees that the Payee designated herein is the proper payee for this Agreement.

IN TESTIMONY WHEREOF PharmaNet and Institution have cause this Agreement to be executed as of the last date and year below written.

For PharmaNet LLC:

Michael E. Land
(Signature) *VP, Worldwide BD*

For Institution:

Nancy Steiger
(Signature)

Name: Nancy Steiger

Title: Chief Executive

Date: 05/28/04

Date: _____

COUNTY OF SAN MATEO

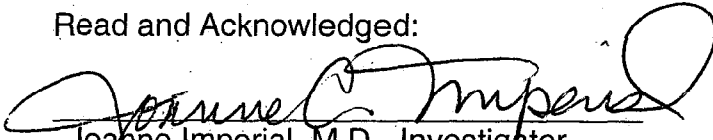
By: _____
Mark Church, President
Board of Supervisors, San Mateo County

Date: _____

ATTEST:

By: _____
Clerk of Said Board

Read and Acknowledged:


Joanne Imperial, M.D., Investigator

Date: 6-24-04

Solely for purposes of acknowledging that it s bound by the obligations under Article 17 hereof:

For Ribapharm Inc.

Name: _____

Title: _____

Date: _____

APPENDIX I – THE PROTOCOL

Date: 27 May 2004
Investigator: Joanne Imperial, M.D.

APPENDIX II – BUDGET AND MILESTONE PAYMENT SCHEDULE

Joanne Imperial, M.D.

The Institution and PharmaNet agree upon the Itemized Study Budget [SEE REPRESENTATIVE SAMPLE ATTACHED BELOW], Appendix III, which lists the monies expected to be earned if the full complement of “qualified” patients is reached. A “qualified” patient means a patient who satisfies the Protocol inclusion / exclusion criteria and completes the entire Study per the Protocol. It is agreed that no reimbursement will be provided for any patients who are enrolled in the Study in violation of the Protocol.

The Itemized Study Budget will be the basis for calculating and reimbursing all Study-related costs. It is agreed that reimbursement will be prorated according to the actual work completed pursuant to the Itemized Study Budget. In other words, costs incurred for all qualified patients will be paid according to the Itemized Study Budget and actual work performed.

Payments will be made in installments, based upon the number of accrued patient visits and in accordance with the following schedule:

Payment Schedule

Initial Payment

Upon execution of this Agreement and submission of regulatory documents =
\$6,685.00

Second Payment

After the randomization of the 2nd patient into the study.

Additional Payments

Will be made on a monthly basis or in accordance with the monitoring frequency at the site based on patient accrual rate.

Payments will be pro rated based on the number of monitored CRF visits. All payments will be proportional to the work performed for the visit.

Final Payment

Will be made upon completion of all monitored CRFs, resolution of all DCFs and reconciliation of Payment #1 versus actual payments.

Screen Failures

Will be paid as per Screen Visit (maximum of 5 screen failures/site).

Reimbursement

One Time Fees, as listed in Appendix III will be paid upon submission of original invoice to PharmaNet.

The total amount to be paid (Total Grant) will be determined based on specific work performed on a pro-rated basis according to the Itemized Study Budget. The Final Payment above will equal the Total Grant less the total already paid. If overpayment by PharmaNet has occurred, upon request, the Institution and or Investigator will immediately refund any such overpayment.

Should the total number of qualified patients enrolled onto the Study be different from the total estimated patients, then (i) in the case of an increase in qualified patients, the Total Grant shall be increased according to the payments described above, and (ii) in the case of a decrease in qualified patients, the Total Grant shall be decreased according to the payments described above and as set forth in the Itemized Study Budget

Institution and Investigator acknowledge the Total Grant represents an estimation of Institution's and or Investigator's total expenses for completion of the Study. In the event of early termination of the Study Institution and Investigator will cancel all cancelable expenses and otherwise use their best efforts to minimize costs and return to PharmaNet any portion of the Total Grant paid to them which is unspent and or unearned.

Payment may take up to six (6) weeks from the date of achieving the milestone.

STUDY PROCEDURE	Screen Visit	Day 1	TW1	TW2	TW4	TW8	TW12	TW18	TW24	TW30
Medical History	100									
Physical Exams (Inc. Fundoscopic Exam at Screen)	200						100		100	
Physical Assessments		50	50	50	50	50		50		50
ECG	75									
Chest X-ray	100									
Vital Signs (1)	20	20	20	20	20	20	20	20	20	20
Adverse Event Review			25	25	25	25	25	25	25	25
ConMed Review	25	25	25	25	25	25	25	25	25	25
Lab Phlebotomy/Processing (2)	35	35	35	35	35	35	35	35	35	35
Pregnancy Test	15	15			15	15	15	15	15	15
Investigator Fee	75	75	75	75	75	75	75	75	75	75
Coordinator Fee	125	125	125	125	125	125	125	125	125	125
Pharmacy Fee/Dispensing		25	25	25	25	25	25	25	25	25
Patient Reimbursement	40	40	40	40	40	40	40	40	40	40
TOTAL / VISIT	810	410	420	420	435	435	485	435	485	435

Per Gen 1,4,5,6,U,M patient (TW48+FU24+2PK) 8,450.00
Per Gen 2,3 patient (TW24+2PK+FU) 6,685.00

(1) includes BMI/weight
 (2) fee X 4 samples for each PK day \$140 per PK day / patient
 (3) W48/72 needed only when patient early terms.

ONE TIME FEES
 IRB/IEC Submission 2,500.00
 Pharmacy Set-up 1,000.00
 Long-Term Document storage 1,250.00

PASS THROUGH INVOICES
 Liver Biopsies

* Screen Failures will be paid as per Screen Visit (maximum of 5 screen