May 19,

RE: Request for Proposal ("RFP") - Clinical Trial Study Management for "Phase II Study of for the Treatment of Patients with Severe Acute Pancreatitis"

Dear Ms.

. Corporation would like to invite
. to submit a proposal and cost estimate for conduct of a Phase 2 clinical study in severe acute pancreatitis. As you know, . a biotechnology company that is focusing on discovering and developing new pharmaceuticals for inflammatory conditions and related diseases.

This study will evaluate the effects of recombinant human
. in patients with severe acute pancreatitis. ,r
, , is a potent pro-inflammatory phospholipid with diverse biologic effects. Corporation is developing . as an agent for treatment of patients with severe acute pancreatitis.

We are seeking a full-service contract research organization (CRO) that has the capability to manage and perform site coordination, site initiation, on-site monitoring, randomization, site contracting and payment management, biometrics, data management and reporting services and management of central and core laboratory services.

This RFP consists of an introduction, the proposal instructions, a protocol synopsis, work breakdown, timeline and contractual terms and conditions. All instructions and requirements should be followed to ensure that a proper evaluation can be performed. The information furnished in your proposal must address the specific items listed but may also include any additional data you consider relevant to the RFP and meeting the needs of .

This RFP contains information which is confidential to . and must be handled in accordance with the terms and conditions in the Confidentiality Agreement which has been signed by and

Nothing in this RFP shall be construed as an obligation by you or to enter into a contract or other business relationship together in connection with the subject matter of this RFP.

The anticipated schedule for this proposal and selection process is as follows:

- RFP Response due back to June 3,
- RFP Award June 19,
- Finalized Contract and Statement of Work July 31,

Your completed proposal should be delivered in person or by express delivery to the undersigned no later that 5:00 PM, June 3, Proposals received after this time may not be considered.

Please acknowledge your receipt of this RFP. If you do not plan to respond, I would appreciate your notifying me as well. Between receipt of this document and Thursday, May 20th, you may contact me at or email for questions. Questions coming after May 20th should be directed to at email

Again, thank you for your interest in and this Study. We look forward to receiving your response.

Sincerely,

Clinical Research Associate

Enclosures

cc:

Request For Proposal (RFP) Instructions

In support of this clinical study, requires the services as outlined in Attachment 4, Task and Responsibility List. In preparing your proposal, please adhere to the instructions and conditions contained in this RFP. The following instructions and conditions are intended to assist you in the preparation and submittal of a response to the RFP.

Please submit the proposal as outlined below:

1. Project Management Approach: Please provide an overview of your project management approach in general and how it would be applied to this study. The names of the project manager and team members who would be committed to the project should be included and their CV's submitted with the RFP.

2. Past Performance and Company Information: Please provide the information required to complete Attachment I, Vendor Information and Qualifications.

3. Statement of Work: Attachment IV, Task and Responsibility List, details the scope of work. may elect to contract for these items individually, in any combination or collectively.

   Alternative or additional services and products which meet the needs of the project may also be proposed. Such products and services should be identified clearly as additional or alternative and should include all relevant information for each product or service proposed, including but not limited to (i) a detailed description of the product or service, (ii) effect on the schedule, (iii) pricing information, and (iv) specific RFP item affected or replaced.

   Note: Refer to Attachment VI, Data Management Requirements for Contract Organizations when pricing the data management portion (items 16-20) of this RFP.

4. Pricing: Submit the budget in a format that **details the price per task** as outlined in the Task and Responsibility List. Where possible, a per unit cost and extended line item cost should be provided (an example would be Project Management at $1,000/month extended to $12,000 for a 12 month project or data management services priced based on a per CRF unit cost. Estimated pass-through expenses are also required.

   A second price format should be submitted using the Resource Allocation Worksheet, Attachment 5. The cost per personnel assigned to each task should be given by FTE, rate/hour and the total (an example is a CRA @100% FTE for 12 months @ $30.00/hr totals $62,400).

   Note: Total amounts for each format should be the same.

5. Contracts: It is ' intent that any proposal which is awarded as a result of this RFP process will be governed by the Master Services Agreement provided with this RFP as Attachment 7 or such other agreement which has been negotiated previously with your company. In the event exceptions are taken to these terms and conditions or any

other contractural requirements contained in this RFP, such exceptions must be clearly stated in your proposal. All exceptions must be identified by section, paragraph, and line(s) of the agreement as appropriate, with clear justification for the exception. Alternatives and/or resolutions for each exception taken should be proposed. Any exceptions will be a consideration in evaluating the proposal and are therefore requested to be kept to a minimum.

6. Other:

   Site Visit: During the proposal evaluation period, an . ; team may visit your organization at your facility(ies) or any proposed sub-contractors or may request that your team or sub-contractor provide a briefing at ; in order to better understand your proposal.

   Ancillary Service: This protocol assumes the use of a central laboratory. Please include any information you wish to be considered regarding central laboratory service providers with which you have an established relationship and the nature of the relationship.

   Administrative: Please submit five (5) unbound copies of your proposal.

If your proposal is to be submitted to on an "all or nothing" basis, this should be clearly indicated in your response to the RFP.

Upon completion of the evaluation process, your organization will be notified in writing.

Attachments

I - Vendor Information and Qualifications
II - Study Synopsis
III - Study Overview
IV - Task and Responsibility List
V - Resource Allocation Worksheets
VI - Biometrics Division-Data Management Expectations for Contract Organizations
VII - Master Services Agreement

Attachment I: Request for Proposal

VENDOR INFORMATION AND QUALIFICATIONS

1. Background Information

Company Name: _____

Parent Company: _____

Other Divisions : _____

Street Address: _____

City, State, Zip: _____

Telephone: _____

Fax: _____

Ownership: Publicly held Privately held

Year Founded _____

Contact(s): _____

_____

_____

2. Financial Information

Attach additional sheets as necessary

(**NOTE** All financial information will be held in strict confidence. If desired, financial information or questions may be directed separately to Robin Moore, Business Manager - Clinical Affairs.)

Banking References:

- Institution Name and Contact Information

Financial Statements

- Balance Sheet
- Income Statement
- Statement of Cash Flows

Dun & Bradstreet Report, if available

Attachment III: Request for Proposal

STUDY OVERVIEW:

Institutional Review Board	Sites will use their local IRB
Study Duration	10 month enrollment; 28 days/pt
Site Qualification Visits & Time on Site	1 visit per site; a total of 34 visits to qualify 30 sites; an average of 5 hours per visit
Investigator Study Start-up Meeting	A 1.5 day meeting with a session on Friday evening concluding on Saturday, the meeting will be held in September 1998
Site Initiation Visits & Time on Site	1 visit per site for a total of 30 visits; an average of 6 hours per visit
Number of Patients	300 (150 per arm)
Number of Sites	Approximately 30
Site Monitoring Frequency	Approximately every 8 weeks or per every 1-2 patients enrolled
Interim Monitoring Visits & Time on Site	8 visits per site for a total of 240 visits; an average of 16 hours or 2 days per visit
Close-out Visits & Time on Site	1 visit per site for a total of 30 visits; an average of 12 hours or 1.5 days per visit
Pharmacy Monitoring Frequency	Initial visit after 1-2 patients enrolled then approximately every 8 weeks or per every 4-6 patients enrolled
Pharmacy Monitoring Visits & Time on Site	4 visits per site for a total of 120 visits; an average of 4 hours per visit
Number of SAEs Anticipated	Approximately 200
Case Report Forms	Approximately 50 pages per patient
Data Management	Approximately 15,000 CRF pages total
Interim Efficacy Analysis	Performed after completion of 150 pts.
Statistical Analysis	CRO to perform a final statistical analysis of the data to *include 30 tables, 23 listings, and 5 figures*
Clinical/Statistical Report	CRO to write integrated report

STUDY TIMELINE:

Activity/Milestone	**Duration**	**Approximate Start Date**
Site Screening/Selection	2 months	July
Study Start-up (IRB approvals)	2 months	August
Site Initiation Visits	2 months	September
Patient Enrollment	10 months	September
Last Patient Visit	na	August
Study closeout	2 months	August
Locked Database	1 month	September
Statistical Analysis	1 month	October
Final Integrated CSR	1 month	November
Estimated Total Duration	17 months	

This timeline is based on approval of the protocol by the FDA and IRB and patient accrual.

Attachment IV: Request for Proposal

TASK AND RESPONSIBILITY LIST:

IMPORTANT: As described in the RFP Instructions, please provide pricing for each line item outlined in the Task and Responsibility List below.

ITEM		CRO
1 - Regulatory		
Provide Investigator Brochure	X	
Prepare annual IND updates	X	
FDA communications related to study	X	
Compile/submit documents to FDA	X	
Site Registration	X	
IND Safety Reports	X	
2 - Protocol Preparation		
Study design	X	
Write protocol	X	
Draft informed consent	X	
3 - Case Report Form Preparation		
Design case report forms to ICOS standards		X
Print case report forms to ICOS standards		X
4 - Pre-study Preparation		
Identification of potential investigators	P	X
Site evaluation visits/reports		X
Site selection		X
IRB submissions		X
Collection of site regulatory documents		X
Submit site registration documents to sponsor		X
Prepare study manual		X
Supply sites with study materials/documents		X
5 - Investigator Meeting		
Plan investigator meeting	P	X
Conduct investigator meeting	P	X
6 - Study Initiation		
Develop site regulatory binders		X
Conduct initiation visit at each site		X
Provide initiation visit report for each site		X
7 - Site Monitoring		
Conduct on-site monitoring visits every 8 wks. or every 1-2 pts		X
Check/verify 100% of CRF's against source documents		X
Provide written report		X
Maintain weekly telephone contact with study sites		X
Provide telephone reports		X
Maintain study regulatory binder		X

P = Primary

3. Services Offered

Attach additional sheets as necessary

Service	Yes	No	Through 3rd party supplier	Comments
Case Report Form Production				
Central IRB				
Purchasing				
Packaging				
Labeling				
Distribution				
Computer Systems Development (*describe system*)				
Consumer Product Testing				
"Central" Contract Laboratory				
Data Management				
GCP Monitoring				
Outcomes Research				
Informed Consent drafting				
Inpatient Phase I facility(ies)				
Investigator Budget Negotiation				
Investigator Grant Administration				
Investigator Meeting Planning				
Investigator Recruitment/Qualification				
Medical/Technical Writing				
Dossiers				
Final Reports				
Manuscripts				
NDAs				
Protocol Development				
Protocol Feasibility Analysis				
QA/compliance Auditing				
Randomization Schedule Generation				
IVRS				
Regulatory Submissions				
INDs				
Investigator Documentation				
NDAs/MAAs/PLA				
IND Safety Reports				
Safety Reporting (AEs, SAEs)				
AE and SAE				
Clintrace for SAE Reporting				
Ability to Transfer Data to ICOS				
Statistical Analysis				
Remote Data Entry (describe system)				
Other (specify)				

4. Business Focus (identify percent of business ot category)

	Pre-Clinical	Phase I	Phase II	Phase III	Phase IV	Rx to OTC Switch	Consumer Medicines	Laboratory Testing	Regulatory	Statistical Analysis
%										

Identify three (3) closest competitors in your *primary* business focus:

1 _____

2. _____

3. _____

Identify three (3) closest competitors in your *secondary* business focus:

1 _____

2. _____

3. _____

Identify your core competencies:

_____

2. _____

3. _____

4 _____

Describe the characteristics and/or services that differentiate you from your competitors (be as specific as possible):

1. _____

2. _____

3 _____

4. _____

5 Clinical Trial Management Experience

Please provide the following:

1 A description of study(ies) your company has conducted in a setting and/or specialty similar to the trial being proposed ~~(critical care, GI, pancreatitis~~) since 1994. Include the specific indication, phase, number of patients, and number of sites (domestic vs. foreign).

2. Describe the role your company had in conduct of those study(ies). eg., complete project management, monitoring only, data management only.

3. Describe your plan for identifying appropriate sites/investigators for the study proposed in this RFP.

6. Business Organizational Structure and Related Information

List Board of Directors

Attachment II: Request for Proposal

STUDY SYNOPSIS:

Study Title: Phase II study of , for the treatment of patients with severe acute pancreatitis

Study Objectives: Determine if treatment with decreases the incidence and extent of multiple organ dysfunction syndrome (MODS) in patients with severe acute pancreatitis

Compare survival time over 28 days and point mortality at Day 28 between treatment groups

Evaluate the effect of treatment on medical resource utilization (e.g., ICU and hospital lengths of stay, major procedures, medication utilization, etc.)

Characterize safety and pharmacokinetic behavior of in critically ill patients

Study Design: Randomized, double-blind, placebo-controlled, multicenter, parallel treatment groups

Approximately 300 patients (150/treatment group) will be randomized to one of two treatment groups:

Group	Number of Patients	Treatment Group
1	150	Placebo
2	150	5.0 mg/kg

Test Agent: is the recombinant form of human , a naturally occurring enzyme which degrades , an inactive metabolite. The placebo contains the formulation vehicle for

Placebo: Formulation vehicle for

Efficacy Assessments: Determine incidence and extent of MODS (Crit Care Med 1995;23:1638-52) over the 28 day study period

Calculate survival time over 28 days by capturing date and time of death in patients expiring

Assess the economic profile of when administered as a treatment for severe acute pancreatitis by comparing the relative medical resource consumption between treatment groups

Safety Assessments: Safety endpoints will include reporting and tabulation of adverse events and clinical laboratory parameters (i.e., hematology, biochemistry, and urinalysis) and assessment of

	the potential immunogenicity of . Interim analysis to assess safety and efficacy will be performed on one occasion
Key Inclusion Criteria:	Onset of abdominal pain ≤ 48 hours prior to initiation of treatment with test article
	Serum amylase or lipase concentration ≥ 3 times the upper limit of normal
	Clinical evidence and diagnosis of acute pancreatitis
	APACHE II Score ≥ 6
Test Agent Administration:	10 minute IV infusion daily for five consecutive days
Frequency of Evaluations:	Baseline (≤ 24 hours prior to first dose of test article), daily on Days 1-7, Day 14, and Day 28
Laboratory Tests:	To be performed by local and central laboratory
Duration of Patient Participation:	28 days
No./Location of Sites:	30 sites located in the United States
Start of Patient Enrollment:	3Q98
Monthly Enrollment:	A minimum of 1-2 patients/site/month
Enrollment Duration:	Approximately 10 months
Project Duration:	Approximately 17 months
Outside Services:	Central Laboratory Drug packaging and distribution
No. of CRF Pgs./Pt.:	50

RESOURCE ALLOCATION

The Resource Allocation Worksheet should be completed as shown in the example below.

RESOURCE ALLOCATION WORKSHEET - EXAMPLE					
ACTIVITY	PERSONNEL	EFFORT	RATE	TOTAL	ASSUMPTIONS
17. Data Entry	Data Entry Operator	400 hrs	$45/hr	$18,000	Double keyed and verified
	Data Entry Supervisor	20 hrs	$60/hr	$1,200	
	File Clerk	40 hrs	$40/hr	$1,600	Includes entry of hard copy lab sheets

Do NOT complete the shaded items.

RESOURCE ALLOCATION WORKSHEET					
ACTIVITY	PERSONNEL	EFFORT	RATE	TOTAL	ASSUMPTIONS
1. Regulatory					
2. Protocol Preparation					
3. Case Report Form Preparation					
4. Pre-study Preparation					
5. Investigator Meeting					
6. Study Initiation					

RESOURCE ALLOCATION WORKSHEET (cont.)					
ACTIVITY	PERSONNEL	EFFORT	RATE	TOTAL	ASSUMPTIONS
7. Site Monitoring					
8. Pharmacy Monitoring					
9. Site Closeout					
10. Drug Supply and Distribution					
11. Laboratory					
12. Serious Adverse Event Reporting					
13. Regulatory Compliance Monitoring					
14. Site Business Management					
15. Project Management					
16. Database Design, Validation, Transfer					
17. Data Entry					

RESOURCE ALLOCATION WORKSHEET (cont.)					
ACTIVITY	PERSONNEL	EFFORT	RATE	TOTAL	ASSUMPTIONS
18. Data Cleanup					
19. Generation and Review of Tables					
20. Additional Data Management Services					
21. Statistical Plan and Analysis					
22. Clinical Reporting Services					