

## PHASE IIB-III

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# PHASE IIB-III: TABLE OF CONTENTS

## ■ PHASE IIB-III

<b>OVERVIEW.....</b>	<b>1</b>
<b>SERVICES.....</b>	<b>2-11</b>
• Biostatistics.....	2
• Clinical Monitoring.....	3
• Feasibility Studies.....	3
• Data Management.....	4
• Interactive Response Technologies (IRT).....	5
• Medical Writing.....	7
• Project Management.....	7
• Protocol/Case Report Form Design.....	8
• Patient Recruitment.....	9
• Global Safety and Pharmacovigilance.....	11



# PHASE IIB-III: OVERVIEW

## GLOBAL PARTNERS. TRIAL EXPERTS.

PharmaNet is a global drug development services company combining solid local infrastructure with a worldwide network of resources. This allows us to efficiently conduct clinical trials from a single study to comprehensive drug development programs spanning multiple continents.

PharmaNet's global footprint, rapid patient recruitment, and therapeutic expertise are just what you need to effectively move your drug or device through the drug development process. In addition to decades of experience in clinical trial design, PharmaNet offers a flexible management style that brings together exactly the team you need, including experts in oncology, cardiology, infectious disease, neuroscience, pain, dermatology, ophthalmology, and other therapeutic areas.

Global experience and a commitment to quality and client service ensure that trials in varied locations and cultures will provide clean, accurate data for analysis. A full range of services, including bioanalysis, data management, biostatistics, project management, study monitoring, patient recruitment, and global safety and pharmacovigilance means that for trials of any size, *PharmaNet works for you.*



## PHASE IIB-III: SERVICES

### BIostatISTICS

PharmaNet biostatisticians have a broad knowledge base in all aspects of clinical trials, from sample size calculation and design specifications during planning stages, to analyzing, displaying, and interpreting data in the final stages of the study. These dedicated professionals include Ph.D.- and MS-level statisticians and statistical programmers located in North America, Europe, and Asia who adhere to a single set of global standard operating procedures and have detailed knowledge of worldwide regulatory agency requirements. We will plan the analyses you'll need before the study begins, then provide reports, statistical summaries, and efficacy and safety analyses promptly and accurately as the study progresses.

PharmaNet pharmacometrics experts can also utilize more advanced techniques for population PK analysis through medical and biostatistical modeling and biomarker and clinical outcomes simulations. We can provide assistance with PK/PD models of clinical studies for innovative and generic products.

During 2010, the Company made significant investments in the implementation of PKS™, WinNonlin®, and WinNonlin® Autopilot™, a complete PK/PD data management and reporting solution. These pharmacometrics tools efficiently extract knowledge from study data to support the sponsor's timely and efficient planning and decision-making.

Refinements to adverse event profiles, biomarkers, and clinical outcomes models from Phase IIa study results

can be used to help design Phase IIb studies. The data can be merged with the previous studies' PK data to extrapolate sound PK parameters and provide robust exposure-response models.

If a pharmacometrics approach has been used throughout the development process, enough information should be available to perform clinical trial modeling that takes into account the PK/PD, efficacy, and patient characteristics, or to simulate a full-fledged Phase III study *in silico*.

### Biostatistics clinical research services include:

- Protocol development, including sample size and power calculations
- Randomization schedules
- Statistical analysis plans
- Statistical programming in SAS®
- Statistical analyses using current methodologies
- Interpretation and reporting of data for clinical trial reports and publications
- Regulatory representation
- Interim analysis and DMC support
- Database integration (ISS/ISE preparation)
- Clinical outcomes modeling to evaluate study designs in order to assess the impact of dosing strategies, patient selection, and clinical endpoint selection
- Medical and biostatistical modeling
- Biomarker and clinical outcomes simulations
- Therapeutic monitoring and population response models

# PHASE IIB-III: SERVICES

## CLINICAL MONITORING

Because the success of your clinical trial depends on the quality of the investigators selected to conduct it, PharmaNet identifies the best sites for your study and provides the management and support necessary for these sites to excel. Upon selection, the sites work with a dedicated clinical trial manager who provides organization, support, and guidance throughout the course of the study.

With decades of experience in global trials, we've built a substantial database of high quality sites with access to patients in a variety of therapeutic areas. We are also continually updating our list through industry outreach, databases, and comprehensive advertising/marketing tactics.

### Clinical monitoring services include:

- Study procedures development
- Source document review
- Patient eligibility confirmation
- Patient compliance tracking
- Supply inventory management
- Adverse events reporting
- Regulatory compliance monitoring
- Regulatory documentation maintenance
- Assist site with patient enrollment and retention strategies
- Frequent contact with sites to address questions and to keep personnel motivated

## FEASIBILITY STUDIES

With regulatory authorities requiring more clinical data, increasingly complex protocols, and difficult challenges of recruiting patients and qualified investigators, early and careful evaluation of your protocol and recruitment plans can help avoid costly missteps.

PharmaNet feasibility studies will help you identify strategies to mitigate the costs and risks associated with a particular trial. A PharmaNet feasibility study will validate whether the protocol has been designed to meet global requirements. Our Medical and Scientific Affairs team also provides input to feasibility studies reviewing potential medical concerns from investigators and commenting on the overall feasibility of the protocol. A PharmaNet feasibility assessment helps identify the best sites and/or countries in which to place the study, and provides meaningful insight into the potential challenges of multicultural recruitment, the impact of competitive trials, patient access, medical infrastructure, staff experience and expertise, and regulatory timelines.

Early identification of potential obstacles enables changes to be made before a costly amendment is required. Our significant experience conducting feasibility studies across a variety of therapeutic areas allows us to provide the quality data and global insight you need to make decisions.

# PHASE IIB-III: SERVICES

## DATA MANAGEMENT

Without clean, reliable data, no trial can be successful. That's why PharmaNet makes data integrity a top priority. PharmaNet's global data management professionals work with you to develop an optimal strategy for managing each project's data. We'll develop a plan to efficiently capture, store, clean, and analyze project data, with stringent quality-control measures to ensure compliance with 21 CFR Part 11 regulations.

### Systems utilized by PharmaNet include:

- Oracle Clinical™ 4.5.1 and 4.5.3
- SAS®
- CRF's Work Manager 5.0
- Medidata's Rave®
- Phase Forward Inform®
- PDS Express and DSG eCaselink

Our six dedicated data management centers in the US, UK, and India follow the same standard operating procedures to ensure global consistency, optimal workflow, and efficient business processes. PharmaNet offers a comprehensive range of data management services for studies conducted by both electronic and traditional paper methods.

### Services include:

- Consultation on strategies, systems, databases, procedures, and metrics
- Case Report Form design
- CDISC compliance
- Database design, validation, and implementation
- Data capture via keyboard entry, fax, and EDC
- Data validation, review, and cleaning
- Medical coding using both standard dictionaries, such as MedDRA and WHO-DD, and proprietary sponsor dictionaries
- Safety procedures, including SAE reconciliation and the management of protocol violations, deviations, and endpoints
- Quality Assurance (QA) processes at each step to ensure high-quality deliverables
- Data consolidation, migration, and conversion
- Management of data from third-party vendors, with automated transfers between external systems
- Development of study specific data management plans

# PHASE IIB-III: SERVICES

## **INTERACTIVE RESPONSE TECHNOLOGIES (IRT)**

PharmaNet's advanced suite of Interactive Voice Response Systems and Web Response Systems (IVRS/ IWRS) or Interactive Response Technologies (IRT) automate management of inventory for drug, device, and clinical supplies, and offer easy-to-use support for randomization, reporting, and electronic patient diaries. All of our IRT services are customized to meet your specific trial needs to automate processes, provide 24/7 service, and produce the necessary reports in the required formats. All service options, such as screening and randomization, are available via the IVR and/or the Web-based IWR.



## ***Inventory Management Services***

- Automated ordering with manual override option
- Drug assignment incorporating titration as necessary
- Real-time access to inventory data via Web reports
- Management of drug expiration dates and drug reconciliation
- Just-in-time distribution of inventory worldwide
- Alerts to remind authorized study staff to place an order

## ***Randomization Services***

- Randomization confirmation via email and/or fax
- Real-time access to subject-related information
- Pre-established, configurable limits to control enrollment
- Flexibility to accommodate adaptive designs
- Multilingual IVRS systems
- 24/7 emergency un-blinding service to authorized individuals
- Warnings to study staff of critical conditions and/or milestones achieved

## ***IWRS Service Options***

- Integrates with Electronic Data Capture (EDC)
- Subject-related data can be exported to or imported from EDC
- Case report forms captured via EDC can be automatically uploaded into IVRS
- Real-time access to Web reports and subject or study information

# PHASE IIB-III: SERVICES

## *Web Reports, Event Confirmation Reports, and Email Alerts*

- Web reports for subject and inventory information
- Automated event confirmation faxes/emails
- Automated email alerts for specified conditions
- Web reports downloadable in various formats
- Reports configured for blinded and un-blinded user groups
- Transaction data captured on confirmation reports
- Email alerts configured for specific individuals or specific user groups

## *Diary Services*

- PharmaNet IRT offers diary service for Electronic Data Capture of patient-generated subject responses to trial questions



# PHASE IIB-III: SERVICES

## MEDICAL WRITING

Comprised entirely of scientists, many with doctorates or other advanced degrees, PharmaNet's medical writing team has significant expertise in key therapeutic areas of pharmaceutical and biotechnology clinical development. They work directly with you to ensure consistency with your format and style while maintaining full compliance with regulatory requirements and International Conference on Harmonisation (ICH) guidelines.

Clear, concise, and professional presentation of study findings is an important factor in any development program. Our professional writers can help you with:

### *Clinical Development*

- Clinical study reports
- Integrated summaries of safety/efficacy
- Clinical expert reports
- Application summaries

### *Marketing*

- Abstracts
- Posters
- Symposia publications
- Slide presentations
- Medical education programs

## PROJECT MANAGEMENT

PharmaNet sets industry standards for the quality of our professionals, the tools they use, and the strategies and efficiencies they bring to managing projects. Each study we undertake has a dedicated project manager who is always available to both the study team and the sponsor.

PharmaNet's veteran project managers, who average ten years of experience and are therapeutically aligned, devote significant time and effort to planning and training in the earliest stages of a project. During this time, they set realistic timelines and make sure that every member of the trial team understands his or her role, tasks, and responsibilities. Using the latest technologies to track up-to-the-minute status of study data, project managers are at the hub of an exclusive program of continual assessment, feedback, and improvement.

During the course of a trial, critical turning points are monitored and project manager's responsibilities include:

- Lead the project team and manage its resources
- Coordinate and track project activities
- Serve as liaison between sponsor and project team members
- Create and enforce project timelines
- Ensure adequate training of project team members
- Communicate trial progress to key stakeholders

## PHASE IIB-III: SERVICES

### PROTOCOL/CASE REPORT FORM DESIGN

A protocol or case report form (CRF) that's vague, confusing, or incomplete could cause delays, unnecessary expenses, and compromised data. PharmaNet professionals are highly adept in developing protocols and CRFs — including electronic versions — specifically for your clinical trials, optimized to provide efficiencies in database design, data collection, edit checks, tables, and listings.

Additionally, protocol and CRF development capabilities include:

- Relevant clinical/scientific considerations
- Determination of sample size
- Statistical methodology
- Compliance with worldwide regulatory guidelines
- Streamlined data collection strategies



# PHASE IIB-III: SERVICES

## PATIENT RECRUITMENT

At PharmaNet, our goal is to find you the right patients and qualified study sites to support delivery of effective study results and support smooth completion of your global trials. We utilize modern media-based recruitment techniques, including a comprehensive social media mix, along with a highly-efficient enrollment process that attracts broad pools of quality, prescreened patients, thereby assisting investigators with the entire recruiting, screening, and enrolling process.

Recruitment specialists work as an integral member of the clinical team, supporting monitors and site managers with materials and programs that augment study performance.

### PharmaNet works for you to:

- Support patient identification and evaluation within the site
- Enhance site efficiency
- Facilitate effective communication about the study
- Establish a local referral network
- Build study awareness
- Track your program with periodic metric reporting

To help studies get the attention they need, we develop branded materials and communications for each study and produce materials from the prescreening poster

to branded study-awareness items with complete consistency. The PharmaNet Patient Recruitment Group (PRG) also works directly with sites to identify and engage potential referral sources, including local physician groups and large primary care clinics, and provides communication materials and instruction to help ensure the success of referral activities.

All materials can be easily accessed via a Web portal created specifically for each study to quickly, clearly, and consistently communicate with patients, investigators, sites, and sponsors to support smooth completion of your global clinical studies.

### *Program Branding and Communications*

A program brand provides an easy-to-remember, recognizable identity that helps to build awareness and commitment. Branding your program includes developing a memorable name and logo and consistently using them in all other materials throughout the life of the study. The PharmaNet Patient Recruitment Group (PRG) works closely with clients to create a memorable study brand.

Branded, program-awareness materials keep studies top-of-mind and differentiate them from other studies competing for a medical personnel's time and attention. Materials are directed at not only the investigator and coordinator, but all clinic staff who may be helpful

## PHASE IIB-III: SERVICES

in patient identification. We can also supply materials to communicate your appreciation for the hard work performed, including certificates, e-cards, and desk reminders. Materials are selected based on cultural appropriateness within your budget.

Physicians and nurses also benefit from prepared information on topics such as patient protections, IRBs, the research process, and benefits of study participation. Pre-study Information Folders include the informed consent form, the study brochure, and an overview of the investigational product and related issues. Additionally, information is provided about how research works, patient protections, and other adjunct information to aid patient deliberation. The PharmaNet PRG develops all materials for inclusion in the folder, produces the folders, and manages the logistics to deliver them to each clinical site.

The PRG works with individual sites to facilitate an efficient process of patient recruitment, identification, and chart evaluation based on individual site dynamics and resources. Materials may include small posters that provide key study identifiers and entrance criteria (for nursing stations and charting rooms), prescreening checklist, tools for flagging charts for further evaluation, or laminated quick reference guides.

### ***Advertising and Promotions***

The PharmaNet Patient Recruitment Group (PRG) is experienced in creating cost-effective advertising campaigns targeting patients. The PRG designs and produces highly-focused marketing materials to attract the selected population and tailor these materials for the needs of individual sites. Our media-based recruitment initiatives include television, radio, print, or Web advertising and materials including direct mail programs and public relations.

### ***Referral Network Management***

The PRG works directly with sites to identify and engage potential referral sources, including local physician groups and large primary care clinics that are already cooperative with the research site. Focusing on medical practices that are already cooperative or friendly with the investigator allows communications to be tightly targeted and increases the chance of a positive response. Selecting investigators that are local experts in the targeted therapeutic area plays an important role in the confident referral of patients.

The PRG provides materials and instruction to investigators and site personnel to ensure the success of referral activities. We can provide contact letters, brochures, posters, leave-behinds, and thank you letters for a successful referral program. We can manage reimbursement for venue, food, and drink for investigator meetings.

## PHASE IIB-III: SERVICES

### GLOBAL SAFETY AND PHARMACOVIGILANCE

PharmaNet's Global Safety and Pharmacovigilance team supports clinical trials and post-marketing safety surveillance. The team comprises skilled professionals who are highly experienced in drug safety, pharmacovigilance, and pharmacoepidemiology and who understand the changing regulatory environment.

To manage clinical trial safety, the team provides qualified medical analysis and review of all Serious Adverse Events (SAE), and creates the necessary 21 CFR Part 11-compliant materials for submission to U.S. and international regulatory authorities and data safety monitoring boards (DSMBs).

#### Services include:

- SAE monitoring
- Expedited SAE reports
- SAE safety narratives
- Annual safety reports
- Safety databases
- Interim safety listings
- Risk management strategies





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Phase I-IV

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