

Supporting a Scientific Approach to Clinical Development



Overview

The Charité Research Organisation:

- Autonomous, 100% daughter company from one of Europe's leading university hospitals; Charité - Universitätsmedizin Berlin
- Supports early/exploratory clinical development from First-in-Man thru Phase II
- Operates its own, dedicated, ICH/GCP compliant research unit with a current capacity of 26-30 beds
- Excellent access to patients via Charité clinics and networks
- Employs a highly experienced team of clinical research professionals

Principles

Scientifically Driven

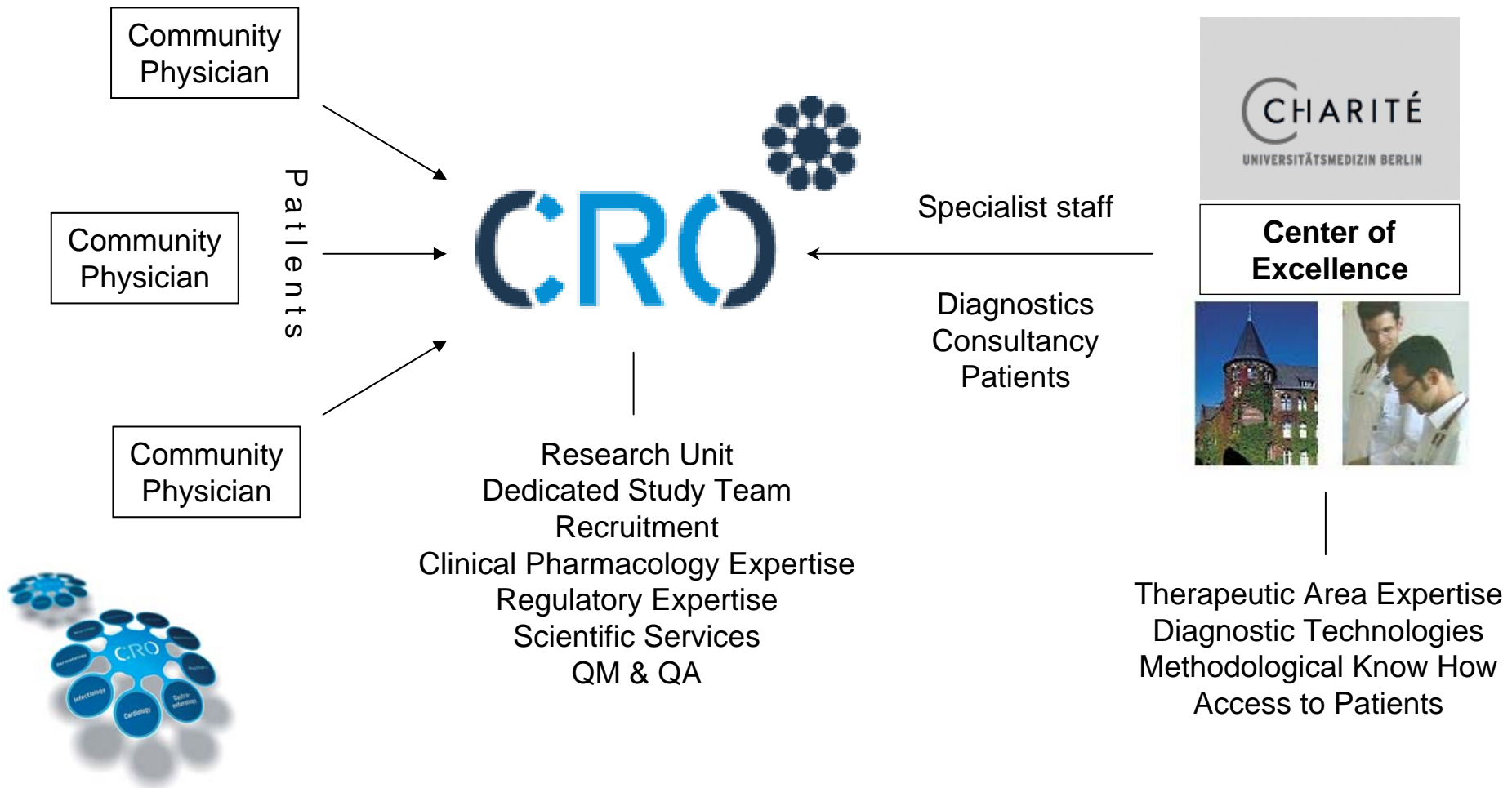
- Support new approaches to early clinical development
- Be capable of implementing complex protocols, not just “feed & bleed” type studies
- Form close partnerships with individual Charité Clinics & Institutes to access patient resources, diagnostic technologies, specific therapeutic area expertise and methodologies
- Be capable of supporting scientific decision making throughout the development process
- Use only experienced study teams

Clinical Development for the 21st Century



- Support “direct into patient” approaches (e.g. monoclonal antibodies)
- Generate greater value in Phase I by investigating very early indications of efficacy through inclusion and evaluation of bio- and diagnostic markers
- Provide infrastructure and expertise (e.g. for safety monitoring boards) to facilitate “fast-track” and adaptive design approaches

Centers of Excellence



Centers of Excellence

Centers of Excellence:

Cardiology	Clinical Immunology
Dermatology	Endocrinology
Gastroenterology	Infectious Diseases
Nephrology	Neurology
Psychiatry	Pulmonology
Rheumatology	Urology



Recruitment

Patient Resources

- The Charité sees in excess of 120,000 in-patients and a further 900,000 out-patients per year
- Charité departments and institutes cover the widest possible range of clinical disciplines
- “Centers of Excellence” approach integrates cooperation with individual clinics
- The Charité name has practically 100% recognition within Berlin and the surrounding area
- The Charité name is trusted and respected
- Patients participate in studies in familiar surroundings

Recruitment

Patient Network

- In addition to recruitment from within the Charité, patients are also recruited from the broader Berlin/Brandenburg community
- Supports recruitment of patients with conditions which are most typically treated by community based physicians, such as:
 - *Asthma & COPD*
 - *Diabetes Type II*
 - *Hypertension*
 - *GERD*
- Recruitment advertising and networking benefits from Charité name, which is instantly recognisable

Charité Research Unit



Facilities

- ICH/GCP compliant research unit with a current capacity of 26-30 beds
- Located in the very center of Berlin on the 20th floor of the Charité Campus Mitte tower
- Used as a clinical research unit since 2000
- Location provides easy access for healthy volunteers and patients in familiar and trusted surroundings
- Close proximity to major clinical departments and institutes supports integration of specialist methodologies and assessments into studies
- Excellent access to world class emergency facilities

Study Types

Examples

- First-in-man studies
- Direct-in-patient / early patient studies
- Dose finding / ranging studies
- PK / PD studies with inclusion / evaluation of bio- & diagnostic markers
- Interaction & challenge studies
- Vaccination studies
- Thorough QTc studies
- Fast-track and adaptive design studies

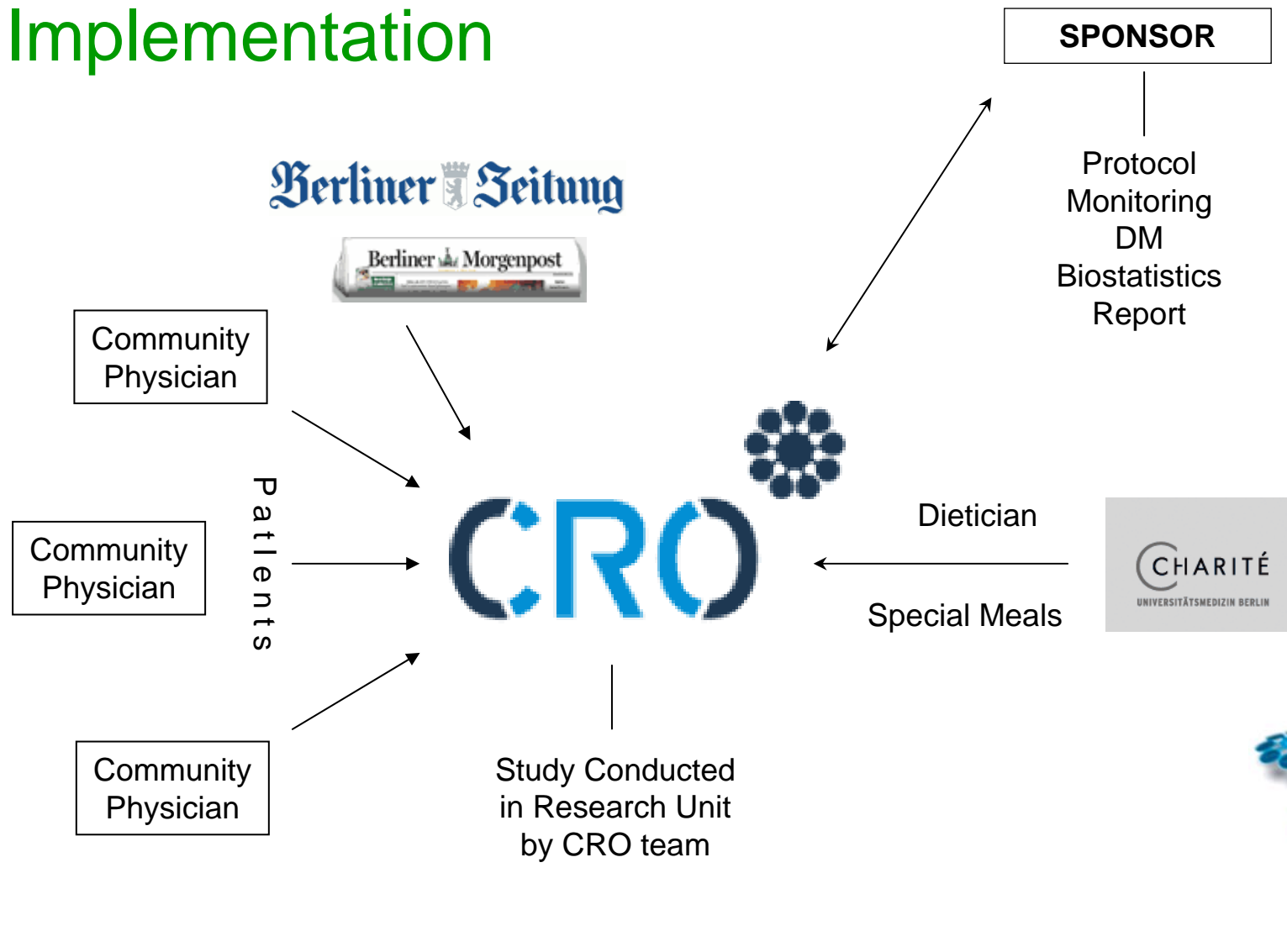
Study Example

Illustrated Example – Diabetes Type II

- Study Overview:** Multiple dose study incorporating up-titration. Study split into 2 cohorts. Dosing period of approximately 42 days, with multiple in-house PK sampling periods.
- Patient Population:** Type II diabetics taking a stable regimen of sulfonylurea or sulfonylurea and metformin. GLP-1 analogue naïve.
- Primary Partner(s):** Multiple private practices across Berlin.
- Support Provided:** Patient referral via networking/press. Dietician, meals.
- Implementation:** Patients treated exclusively in Charité Research Unit by dedicated CRO study team. Best performing center in Europe.



Implementation



Typical Ethics & Regulatory Timelines

- Competent Authority:** 30 days if single center (in Germany)
 60 days if multiple centers (in Germany)
 Fast-track available in some cases where study is part of a program that has already commenced in Germany (i.e. CA is already aware of IMP).
- Ethics:** Central Berlin ethics committee,
 6 sub-committees with 1 meeting each week,
 30 day or less turnaround for single center studies.
- Comments:** Where an initial ethics approval has been obtained elsewhere in Germany (PI site), Berlin ethics only needs to be notified of inclusion of CRO in program.



Charité Research Unit



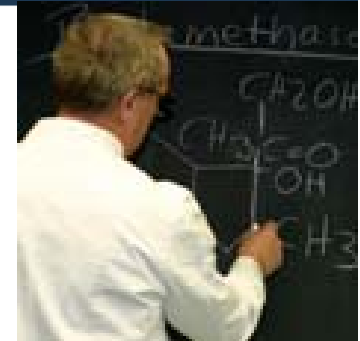
Supported By

- Cooperation with St. Hubertus pharmacy:
 - Experienced in handling clinical trial supplies
 - Own QPs in place
 - Able to prepare investigational products on-site as needed, GMP license
- Cooperation with W&T clinical laboratory
 - Experienced in the conduct of routine clinical laboratory assessments in support of clinical trials
 - Wide range of standard assessments available
- Cooperation with CENiMED, a pharmacogenomics specialist
 - Genotyping

Consulting Services

Examples

- Development planning with regulatory perspective
- Protocol development with input from therapeutic area experts
- Clinical trial reports
- Assessment of current regulatory thinking and expectations
- Expert evaluation of available investigational product data
- Evaluation of the benefits and requirements of/for additional studies
- Assistance with the formation of expert advisory panels



Why Choose the CRO?

Advantages

- Scientifically driven approach facilitates the conduct of complex and “elevated risk” study types
- Business model promotes price competitiveness for “routine” studies
- Access to vast patient resources
- Opinion-leading therapeutic area expertise available
- Cooperation with clinics provides access to methodological excellence and advanced diagnostic technologies
- Research unit located in one of Europe’s leading teaching hospitals with excellent access to emergency care facilities