WORLDWIDE
CLINICAL TRIALS

ACCELERATING YOUR PAIN AND ANALGESIA TRIALS

Last Update: 05012021

ACCELERATING YOUR PAIN AND ANALGESIA TRIALS

The advances in our understanding of pain mechanisms and a large number of clinical studies have not translated into more effective, affordable, and safer pharmaceutical products. But we can change that.

YOUR CRO PARTNER CAN HAVE A SIGNIFICANT IMPACT ON THE SUCCESS OR FAILURE OF YOUR CLINICAL STUDY AND PROGRAM

Worldwide has extensive capabilities in global analgesia research, including experience with human experimental and clinical models for proof-of-concept in nociceptive and neuropathic pain and for registration studies to support marketing authorization in a number of acute and chronic pain indications, including pediatric pain indications.

SPECIALIZATION IN PAIN AND ANALGESIA PROGRAMS FOR ACCELERATED TRIALS

When timing is critical and everyday delays can cost millions, Worldwide's simple, thorough, streamlined operations are critical to your neurology development program.

Worldwide has a dedicated team of pain and analgesia experts — neurologists; experienced clinical monitors and project managers; and regulatory, data management, statistical, scientific, and medical experts — that work collaboratively with you to implement traditional and innovative trial designs that can address important issues in analgesia trials, including heightened placebo response, an increasing number of failed (not just negative) trials, highly subjective and variable endpoints, and a lack of accepted biomarkers.

Worldwide's integrated Clinical Assessment Technologies (CAT) team provides rater training, scale management, and management of electronic outcomes solution vendors. The CAT group is seamlessly integrated with the other functional teams to yield efficiencies in budgets, time lines, communications, common resources, and shared systems, while increasing overall data quality.

> *"Worldwide recently identified a risk that would have affected the continuation of our project, developed a mitigation strategy, and worked closely across functions and with sponsor stakeholders to develop a solution. Not only was the plan well executed by the team, but it also worked!"*
>
> *- Worldwide Customer, Global Project Management*

AWARD-WINNING CRO

Our award-winning, specialized Central Nervous System teams deliver uncommon value, helping emerging and established biopharma, biotech, and pharmaceutical companies test, validate, and de-risk the process of developing better treatments across all pain indications.

CRO LEADERSHIP AWARDS2019

Capabilities, Compatibility, Expertise, Quality, and Reliability

UNCOMMON GLOBAL SITE AND INVESTIGATOR NETWORKS FOR FASTER PATIENT RECRUITMENT

With Worldwide, you get the best of both worlds: A specialized, CNS-focused CRO with global coverage. What does this mean for you? Access to sites, investigators, and patients across the globe, without the hefty price tag and cookie-cutter approach you get from large, consolidating CROs.

+1 610 964 2000 | WORLDWIDE.COM

Last Update: 05012021

WORLDWIDE CLINICAL TRIALS

INDICATION EXPERIENCE

Neuropathic pain

Post-operative pain

Post-surgical pain studies in children aged from birth to >2 years

Combined neuropathic pain for those with chronic post-operative pain

Intractable cancer pain (e.g., intrathecal infusion of conopeptides and epidural injection of NCE)

Breakthrough cancer pain

Low back pain

Migraine

Postherpetic neuralgia

Pain associated with osteoarthritis of the knee

Complex regional pain syndrome for orphan diseases

Central pain in rare disease populations (e.g., Neuromyelitis optica spectrum disorder)

DELIVERING FPI 4 WEEKS AFTER AWARD, WORLDWIDE EXPEDITES STUDY START UP FOR OA KNEE PAIN TRIAL

STUDY OVERVIEW

- Phase IIb, double-bind, placebo-controlled, dose-ranging study to evaluate safety and efficacy of IP in chronic, moderate to severe OA knee pain
- Primary end point: Analgesic efficacy
- Secondary end point: Dose-response, duration of analgesic efficacy, percentage of responders, improvement in physical function, quality of life
- Study conducted at 20 US sites, enrolled 175 subjects
- Worldwide provided full service for this study

CHALLENGES

Critical Requirements

- Constrained timelines
- Stringent eligibility requirements
- Use of patient diaries
- Patient reported outcomes

KEY LEARNINGS

Patient Diaries

- Daily IHCRA calls to sites (held sites accountable for their enrolled subjects' data)
- Ensured proper alerts of ePRO system are set up and seamless EDC integration

Data Issues

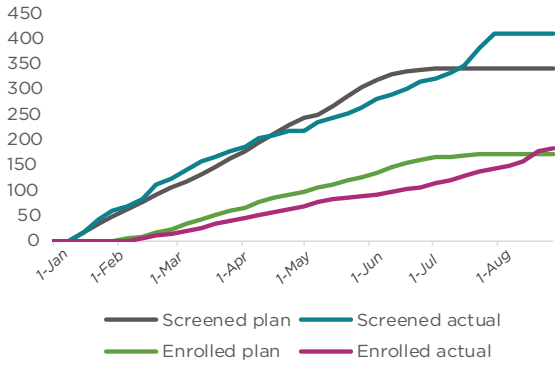
- Implemented re-monitoring plan for 25% of the sites, which produced 50% of the study data
- Conducted medical monitoring with robust and comprehensive patient profile review

High Screen Failure Rate

- Observed high screen failure rates due to eligibility criteria early in the study
- Implemented a protocol amendment and mitigated impact on timelines

KEY SUCCESSES

Study Recruitment



First Patient In Four Weeks After Study Award

Low Drop-Out Rate

Clinical Monitoring

Expedited Site Start-Up

+1 610 964 2000 | WORLDWIDE.COM

Last Update: 05012021

WORLDWIDE CLINICAL TRIALS

CRITICAL OPERATIONAL ISSUES TO CONSIDER FOR ANALGESIA TRIALS

ANALGESIA CLINICAL MEASURES

- Phase I pain models
- Quantitative Sensory Testing (QST)
- McGill Pain Questionnaire
- Brief Pain Inventory
- Neuropathic Pain Scale
- Neuropathic Pain Questionnaire
- Neuropathic Pain Symptom Inventory
- Leeds Assessment of Neuropathic Symptoms and Signs
- University of Michigan Sedation Scale
- Face, Legs, Activity, Cry, Consolability scale

STRATEGY

- Congested landscape in the pain and analgesia space
- Protocol complexity
- Proper placebo allocation optimal ratio for pair-wise contrasts
- Use of inclusion scales

START-UP

- Site selection
- Rater training and qualification
- ePRO development and testing

LOGISTICS

- Scales licenses/ translations/ material
- Use of electronic diaries (ePRO)
- Hospitalizations
- Drug supply chain

CONDUCT

- Recruitment and retention
- Assessment consistency
- Blinding and maintaining site/patient blind
- Patient compliance with electronic diary measures, medication adherence and clinic visits
- Use of rescue drugs

+1 610 964 2000 | WORLDWIDE.COM

Last Update: 05012021

THERE'S NO SUBSTITUTE FOR UNCOMMON EXPERTISE. MEET YOUR PARTNERS.

Worldwide is committed to delivering uncommon value. In fact, we go above and beyond to deliver solutions and services that exceed your expectations. Our collaborative, customized project teams, with phase- and indication-specific expertise, develop successful strategies for even the most novel therapies.

Tamara Ast, Ph.D.

Senior Vice President, Project Delivery Services, Neuroscience

Dr. Tamara Ast has 20 years of industry experience across a variety of neuroscience indications. She has held leadership roles for Project Management and Operations delivery at Worldwide Clinical Trials for the past five years, and now oversees the Neuroscience therapeutic area. This business unit includes Worldwide's most experienced Neuroscience clinical research professionals to ensure that the Worldwide team provides sponsors with the best possible regulatory and scientific, medical and operational strategy and clinical trial execution.

Dr. Ast's primary therapeutic and operational expertise has had a specific emphasis on neurological conditions, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, pain, and psychiatric indications such as schizophrenia, mood disorders, and substance use disorders Dr. Ast obtained her Ph.D. in medicinal biochemistry from The School of Pharmacy, University of London, United Kingdom.

Michael Murphy, M.D., Ph.D.

Chief Medical and Scientific Officer

Dr. Murphy's professional career has spanned 25 years, and his positions within the pharmaceutical industry emphasize the integration of medical and scientific acumen with operational excellence. He is board-certified in psychiatry and has a doctorate in pharmacology, with training at Tulane University, Stanford University, and the Mt. Sinai School of Medicine.

Dr. Murphy worked with Dr. Cutler to articulate Worldwide's vision when the company was established as a global CRO in 1995 and was responsible for consulting services for protocol and program design and executive oversight for the execution, analysis, and interpretation of clinical trials across multiple therapeutic areas.

His supervisory responsibilities as Chief Medical & Scientific Officer at Worldwide are international in scope and include the design and implementation of protocol feasibility assessments, protocol development for Phases I–IV including non-interventional research, the provision of medical monitoring and drug safety services, medical writing, and coordination of rater certification and surveillance activities for clinical trial assessments.

Henry J. Riordan, Ph.D.

Chief Development Officer

Dr. Riordan is responsible for bringing together Worldwide's scientific assets across CNS, General Medicine, Cardiometabolics, and Oncology Franchises and connecting the critical functions that serve to differentiate Worldwide by implementing strategies and tactics consistent with our vision of being the leader in the application of rigorous methodology and medically/scientifically advanced drug development processes producing reliable data to support highly informed health care decisions.

He has been involved in the assessment, treatment and investigation of various CNS disorders in both industry and academia for more than 20 years; was one of the original Worldwide team members beginning in 1998, and a cofounder of the current Worldwide. He has been the primary author of numerous protocols in neurologic, psychiatric and analgesic indications across all phases of development. He has been involved in several clinical development programs and has participated in numerous advisory boards and regulatory interactions. He has advanced training in quantitative methods, biostatistics, experimental design, neurophysiology, neuroimaging and clinical neuropsychology and has published over 120 peer-reviewed abstracts, articles, book chapters and books.

Prior to joining the late phase team he was the clinical lead for Worldwide's early phase development unit, where he was responsible for helping to establish their specialized patient study unit. He also spent several years in the departments of neurology and psychiatry at Jefferson, the University of Pennsylvania and Dartmouth medical schools.