veeda clinical research®

ARIPIPRAZOLE LAI

An overview of Veeda's approach to streamline Schizophrenia Drug Trials

We are now supporting you through all the stages in a drug development continuum

Schizophrenia is a chronic and severe mental disorder that affects a person's thoughts, feelings, and behaviours. This disorder affects a person's perception of reality, social interactions, and thought processes.

Schizophrenia affects 20 million people worldwide.

Our medical, regulatory and operational experts bring their scientific knowledge and global execution capabilities to your program to streamline and accelerate drug approval.

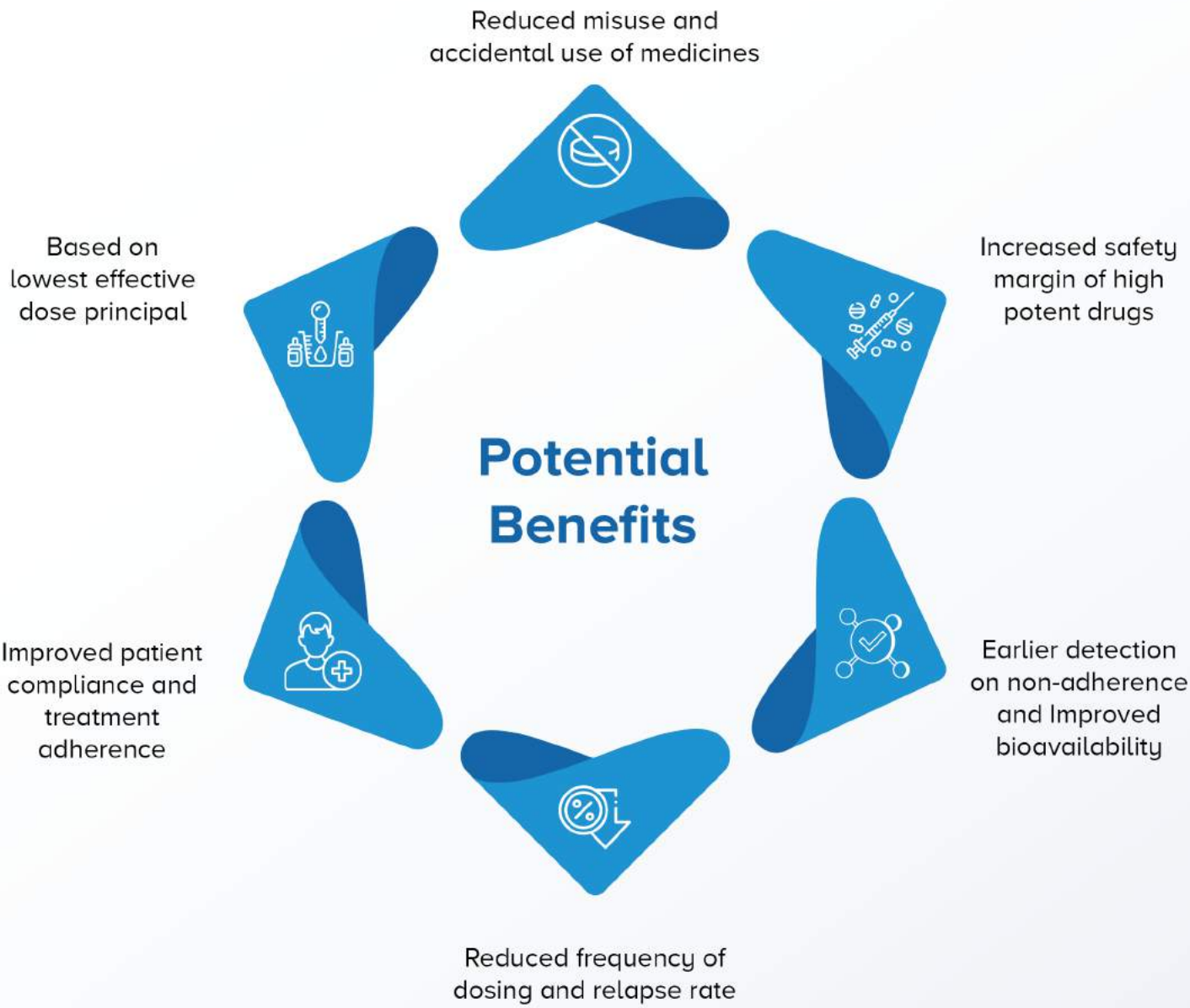
What Makes Schizophrenia a Cause of Concern?

- It is difficult to reverse
- Symptomatic relapses are frequently observed
- Most patients need long-term pharmacological treatment
- Antipsychotic drugs are the mainstay of clinical care
- According to the American Psychiatric Association, second-generation (atypical) antipsychotics (SGAs) are the agents of choice for first-line treatment of schizophrenia

Increasing Importance of Long-Acting Injectable (LAIs)

Formulation	Drawbacks
Oral	▸▸ Time to relapse is less ▸▸ Poor compliance ▸▸ Even oral ER formulations are to be administered daily
Injections	▸▸ Parenteral drug delivery systems - fast drug absorption and rapid elimination ▸▸ In the case of chronic conditions - daily or weekly injections for months or years result in poor patient compliance

Potential Advantages of Long Acting Injectable



veeda clinical research

Pre Study Activities Plan

Month 1

- Customer expectation meeting
- Timeline confirmation and finalization of strategy
- Vendor selection
- Site selections start
- Support Regulatory submission

Month 2

- Full work order executed
- Finalization of protocol
- Vendor contracts executed
- Study plan creation
- eCRF creation
- Database build
- Final site list defined
- Drug distribution plan finalized
- Sites contract negotiation and full execution
- RA, IRB and EC submissions

Month 3

- Electronic data capture (EDC) set up
- Vendor system set-up
- RA, IRB and EC approvals
- Drug ready to ship
- Kick-off meeting

Our Effective Recruitment Strategy that Works Globally!

Month 4-8

- SIV for all sites
- Preparation & Shipment of SIV Kits
- Training of Investigator's and study team during SIV
- Shipment of stabilization medication to sites
- Patient Identification, screening
- Patient eligibility documents review by medical team
- Eligible patient stabilization
- Continuous follow up with sites for tracking patient stabilization activity
- Preparation of SIV reports on CTMS platform and finalize the same within defined timelines after sponsor's confirmation

Month 9-13

- Continuous follow up with sites for ongoing stabilization patients and planning randomization of patients
- Shipment of Investigational Medicinal Product and PK kits to all sites
- First Patient Randomization (FPI)
- Arrangement of trained phlebotomist for PK sample collection, processing and storage at sites
- In process monitoring visit during randomization of 1st patient at each site
- Routine monitoring visit in a frequency of once in month at each site
- Last Patient Randomization (LPI)

Month 14-17

- Follow up with sites for tracking patient visit and to track the IMP and PK sample storage conditions and for completion of source document and e-CRF
- To arrange the shipment of IMP to sites and to arrange the PK sample shipment from sites to Veeda Facility
- Routine Monitoring visit at each sites as per agreement and monitoring plan
- QA audits at all sites as per agreement and QA audit plan
- Data Cleaning, Review of protocol deviation tracker, SAE & AE Tracker
- Preparation of Monitoring visit reports on CTMS platform and finalize the same within defined timelines after sponsor's confirmation

Post Recruitment Activities Plan

Month 18

- Shipment of all PK samples aliquot to Veeda facility
- Data Cleaning and ensuring the data base is ready for data base lock
- Analysis of PK samples
- QA review and confirmation for Data base lock
- Principal Investigator authentication and approval from sponsor for data base lock

Month 19

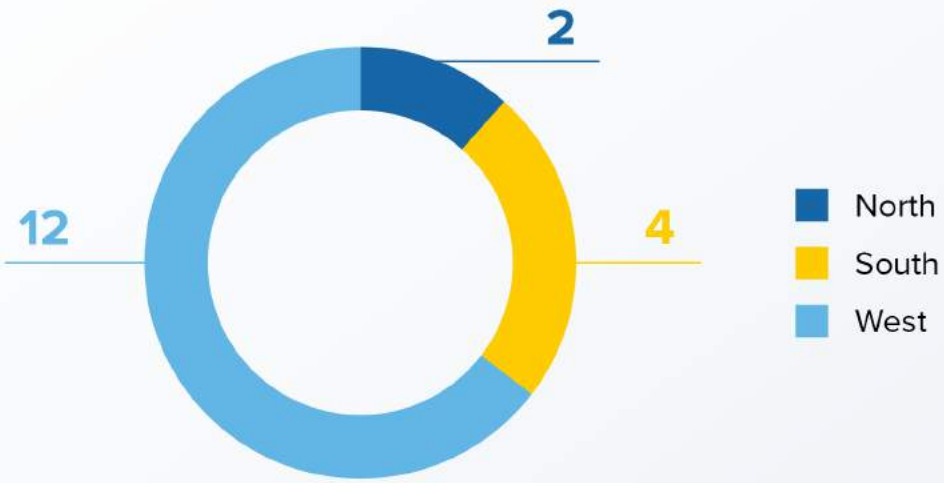
- Data base Lock
- Preparation of table listing and graph
- Statistical analysis of the PK and study result
- Preliminary result with sponsor
- Preparation of draft study report and to share for sponsor's review
- SCV will be completed for all sites after finalization of CSR i.e. in month # 21 and 22 and during SCV all study documents will be archived at sites and IMP retention samples will be archived at third party

Month 20

- Review of draft study report by internal Veeda team and by sponsor
- Finalization of Clinical Study report
- Dispatch of Final Clinical study report to Sponsor

Veeda's Investigator Site Network

We have 15+ investigator sites for Aripiprazole study across India



The investigator sites have experience of **9 USFDA & 6 EMEA studies**

Commitment to Quality: Our Proactive Quality and Compliance Control Plan

- Study specific Quality Management Plan
- Aligned Sponsor and CRO Processes
- Study specific training for CRAs
- Mandatory protocol training with knowledge assessment
- GCP training

Veeda's Focus During QA Audits

- Safety of subjects
- Reporting of AE/SAEs to IRB, Regulatory and sponsor
- Regulatory aspects of the trial such as regulatory and IRB/IEC approval
- Protocol Compliance (including inclusion and exclusion criteria check)
- Availability of current version of all essential documents (such as Protocol, ICD, e-CRF completion guidelines etc.)
- Review of study team training and experience
- Overall GCP and applicable Regulatory Requirements Compliance
- Availability of source data, its accuracy and documentation practice
- Adequacy of resources for the conduct of Study at Site
- Suitability of equipment used during the study (Eg. Calibration)
- IMP accountability clinical trial supplies documentation
- Storage of IMP and PK samples
- Informed consent process and informed consent documents.
- Site Investigator File review
- e-CRF completion
- Deviations occurred at the site
- Interview with Principal Investigator and Site Team
- ICF Verification of All Screened Patients

Global Execution Capabilities for Risk Management

Risk Management Plan

Risk (e.g. process step)	Risk Description	Trigger	Primary Response Strategy	Mitigation
Management of a missed dose	Possibility of Missed Second Initiation and/ or maintenance Dose	Patient visit tracking	Avoid & Mitigate	Protocols design including procedure or steps with window period for management of missed doses Encourage to patient and patient's LAR to comply with dosing scheduled through informed consent and also reminders from sites Follow ups by CRO team
Prohibited Medication	Aripiprazole has the potential for inducing orthostatic hypotension, an additive effect may occur when Aripiprazole is administered with other therapeutic agents that have this potential The concomitant use of Aripiprazole and strong inducers of CYP3A4 and P-gp may decrease the exposure of Aripiprazole	Prescriptions and patent's ongoing treatment	Avoid & Mitigate	List of prohibited medication shall be included in protocol with below points Discontinuation criteria in protocol if required to use of prohibited medication Safety monitoring planning if required to use of prohibited medication Training to in-house and sites staff on protocol Well experienced investigator selection

veeda clinical research

Risk Management Plan

Risk (e.g. process step)	Risk Description	Trigger	Primary Response Strategy	Mitigation
Patient Dropouts	More number of patient dropouts Non-compliance to study requirement	Discontinuation Deviations	Avoid & Mitigation	Site shall be upraised on protocol needs with respect to the patient visits Investigators are requested to enroll patients which can be compliant to the study needs CRO oversight is maintained by continuously tracking patients visit to ensure compliance.
Quality Management	On-line Source documentation High number of deviation on study procedures Non-compliance of ALCOA+ principals	Any site with history of quality issues Observations during CRA visits QA audit observations	Avoid & Mitigation	Inspection history and outcome of inspection consideration during site identification Site practices and SOP evaluation Investigator oversight Re-training to site staff on protocols and GDP requirement-if required CAPA implementation at applicable site