Akros Clinical Development Goal 2015

Jan 27, 2015

JT/AKROS PHARMACEUTICALS CORPORATE VISION

A unique, world-class pharmaceutical business driven by R&D with a solid market presence through original and innovative drugs.

JT/AKROS PHARMACEUTICALS CORPORATE MISSION

To achieve steady progress of clinical trial stage products and place compounds with the potential world-class medicines in clinical development.

AKROS PHARMA GOALS

Link nonclinical efficacy and safety results to those from effectively-designed Phase I/II clinical trials to provide basis for rapid and efficient development through Phase III.

AKROS PHARMA STRATEGIES AND MEASURES

I. Achieve steady progress in developing compounds.
(see Attachment 1)

A. JTT-851

1. **In accordance with out-licensing situation and updated development strategy, Akros will consider to plan and conduct studies.**

B. JTZ-951

1. **Support to establish the development plan in ex-JPN along with obtaining feasibility/budget information of Ph2 studies (007/ND-CKD and 008/HD-CKD studies) in 1Q 2015, which will be utilized for internal decision at LDSC.**
   In case of decision to move the ex-JPN development forward at LDSC, Akros will prepare for Ph2 studies and PRT will be finalized by 4Q 2015.
2. **Plan and undertake any developmental actions for other clinical studies in accordance with the updated development strategy.**

C. JTE-051

1. **Complete topline results of CYP DDI (004 study) in 1Q 2015.**
2. **Prepare and initiate MTX-DDI study (005 study) and complete topline results in 1Q 2015.**
3. **Complete the clinical phase of JP population bridging study (006 study) and complete topline results in 1Q 2015.**
4. **Prepare for Ph2a study (003 study) and initiate it in early 3Q 2015.**

D. JTE-151

1. **Plan and undertake any regulatory or developmental actions in accordance with the updated development strategy and regulatory situation.**

E. JTT-251

1. **Plan and undertake any regulatory or developmental actions in accordance with regulatory situation and the updated development strategy.**

F. JTT-252

1. **Complete the clinical phase of Ph1 SAD study (001 study) in 1Q 2015 and topline results in 2Q 2015.**
2. **Prepare for Ph1 MAD study (002 study) and initiate it in 2Q 2015.**

To assess the performance, please refer to the Akros' benchmark (see Attachment 2).

II. Increase speed and quality of output

1. **Continue SOP Committee, Data Analysis Steering Committee, and Safety Review Committee activities to support clinical studies in Akros.**

2. **The following task force activities are planned in 2015.**

- **CSV Project(Kala/Others)**
  CSV SOPs and Forms (21 documents total) to be finalized by January 2015. Start CSV SOP implementation with target completion by the end of 2015.

- **Organize and facilitate internal QA system (Kala/A. Sophia/Masaki)**
  QA/Compliance consultation will be performed as needed on project basis, but for establishing a higher level of internal QA system, we will start collaboration with contract QA personnel.

- **Conversion of CSR to eCTD Format (A.Bastien/T. Ghaderi)**
  RA/CLR will discuss the process and develop timeline for accomplishing the task. Based on the timeline, tasks starting time will be determined.

- **Akros Data Acquisition and Reporting Standards (K. Pu/A.Bastien/S.Light)**
  This document includes several components, some of which have been finalized. Akros standard eCRF, database and terminology will be maintained in a document that is stored in Documentum. Akros standard edit checks will be maintained in the global library in Rave. The goal is to finalize the remaining parts of ADARS and collaborate with JT team. (Section 2 should be done by Clinical Research).

- **Global eCRF Working Group (S. Light)**
  Akros and JT will update standard eCRF as needed with change control. Akros and JT will develop global therapeutic area specific standards as needed in 2015.

- **Integrated collaboration with Clinical Pharmacology, DMPK, and Tox groups in JT (S. Pai)**
  This working group is to discuss topics for more collaborative and efficient work. Some WPS will be prepared for practical standardization of the field.

- **Human Mass Balance Study Task Force (S. Pai)**
  JT/Akros has not conducted such a study and will start this TF for preparation of upcomoing study. This TF will be formed with the objective of setting criteria, study timing, key decision points, and need, to provide recommendation to therapeutic area teams, upper management, and Steering Committee.

- **DSUR Preparation (RA/CLR)**
  SOP will be finalized by Jan, 2015 and then actual work will start. Selected IND annual reports in DSUR format will be prepared in collaboration with JT and submitted to the FDA.

- **Enhance KOL, Consultant network for Akros projects (A. Bastien)**
  Timely KOL input is vital for CLR to create high quality study protocol and/or clinical development plans. CLR usually obtains and utilizes KOL input as needed. CLR group will analyze the current process of identifying and selecting KOLs. CLR will use this analysis to improve this process and consider it to strengthen the current network.

- **Global study preparation Task Force(Masaki/Others)**
  Work to prepare for global studies and collaboration with JT will start from this year.

- **Improvement of tools and processes for safety and efficacy data review(A. Bastien/S. Light)**
  This TF utilizes Spotfire to produce patient profiles and possibly other reports, for data review. Define a process for inter-departmental data review for P2 studies.

- **Upgrade current process to prepare the qualified study plans and deliverables stably and efficiently (A. Bastien/CLR)**
  CLR will review and upgrade as appropriate current system and process of research and PRT development in order to efficiently produce high quality protocols.

- **Develop tools and guidelines for Phase II start-up activities (A. Sophia)**
  CLO will develop these tools to educate and allow improved and effective proactive planning not only at the start of Phase II, but more importantly during early stage strategic planning. With proper tools and guidances in place, the implementation will be faster and earlier in the process.
  Work on tools and templates to prepare standard guidance at Akros and Work with cross functional team to ensure alignment and accuracy will be initiated in 2015.

- **Develop an electronic Trial Master File system using the Akros Documentum platform (A. Sophia)**
  This TF includes the tasks of (1) Re-define hierarchy and folders for (e) TMF, (2) Select and define eTMF system suitable for Akros, (3) Design & Develop eTMF system

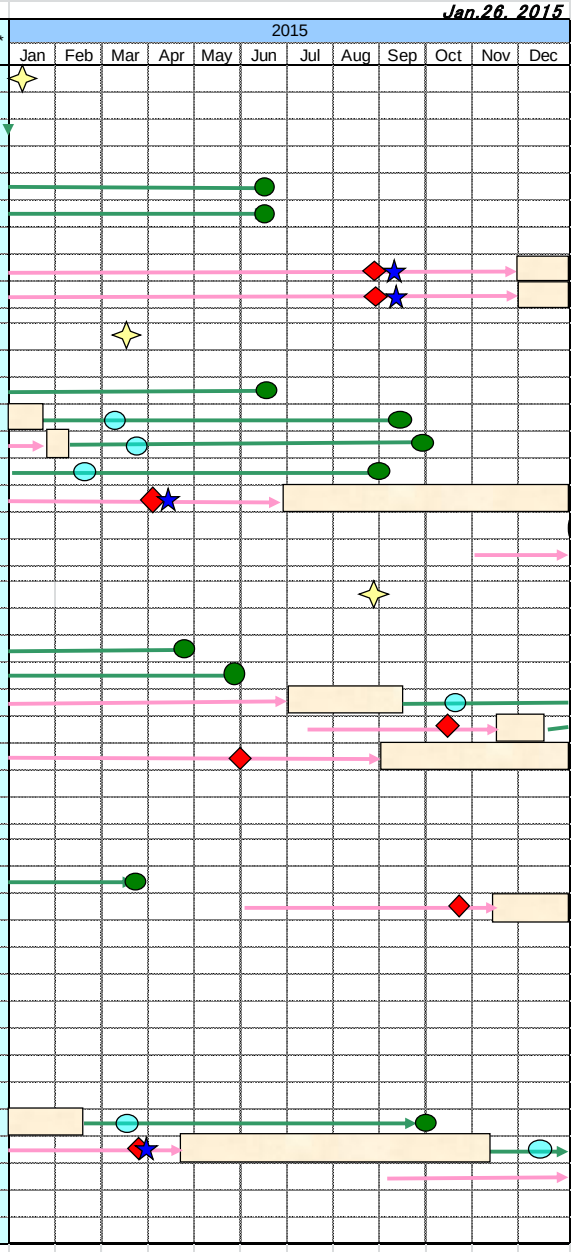
- **JT/Akros joint working group for improvement of clinical development speed (Masaki/Others)**
  This joint WG will start discussion to improve JT-pharma's development speed based on some key topics as well as speed benchmark analysis.

Attachment 1
Akros Study Plan in 2015

Akros Study Plan

Jan.26, 2015

Project	PRT No	Study	Status*
JTZ-951			
JTZ-951	U-11-001	Ph1, SAD, HV	0
JTZ-951	U-12-002	Ph1, DDI, Phosphate Binder, HV	1
JTZ-951	U-12-003	Ph1, MAD, DDI, Cooperstown, HV	1
JTZ-951	U-12-004	Ph1, MAD, HD-CKD	1
JTZ-951	U-13-005	Ph1, SD, HD-CKD	1
JTZ-951	U-13-006	Ph1, MAD, ND-CKD (TBD)	3
JTZ-951	TBD	Ph2, HD Switch/maintenance dose D	3
JTZ-951	TBD	Ph2, ND-CKD, Induction/Swith/Mainte	3
JTE-051			
JTE-051	U-11-001	Ph1, SAD, FE, HV	1
JTE-051	U-13-002	Ph1, MAD, HV	1
JTE-051	U-14-004	Ph1, DDI, CYP2C8 & 3A4, HV	2
JTE-051	U-14-005	Ph1, DDI, MTX, HV	2
JTE-051	U-14-006	Ph1, JPN PK Bridging	1
JTE-051	U-13-003	Ph2, RA PoC Dose-range finding(MT	3
JTE-051	TBD	Ph2b RA Dose-finding(MTX-IR, globa	3
JTE-051	TBD	Ph2 2nd indication Dose-range findin	3
JTE-151			
JTE-151	U-13-001	Ph1, SAD, HV	1
JTE-151	U-13-002	Ph1, MAD, HV	1
JTE-151	U-14-004	Ph1, DDI, CYP, HV	1
JTE-151	U-14-005	Ph1, JPN PK Bridging(TBD)	1
JTE-151	TBD	Ph1, DDI, MTX, HV	2
JTE-151	U-13-003	Ph2, PS PoC, Dose-range finding	3
JTE-151	TBD	Ph2b PS Dose-finding(global)	3
JTE-151	TBD	Ph2, 2nd indication(RA) Dose-range finding	
JTT-251			
JTT-251	U-13-001	Ph1, SAD, HV & T2DM	1
JTT-251	U-14-002	Ph1, MAD, HV	2
JTT-251	TBD	Ph1 DDI CYP induction	2
JTT-251	TBD	Ph1, Phototox	2
JTT-251	TBD	Ph2, DM PoC	3
JTT-251	TBD	Ph2b, DM	3
JTT-251	TBD	Ph1, PoP, HV	2
JTT-252			
JTT-252	U-14-001	Ph1, SAD, HV & T2DM	1
JTT-252	U-15-002	Ph1, MAD, HV & T2DM	2
JTT-252	TBD	Ph2, DM PoC	3
JTT-252	TBD	Ph2b, DM	3



Legend		
		IND (CTA) Submission
		Annual Report or Drug Safety Report
		Study Preparation (IND, Protocol/IDB, Site Start-u
		Final Protocol (4 months preparation time if sched
		Clinical Study Period (FPFV [screening] to LPLV)
		Listing/Table/Report Development
		Summarized Topline Results (2 months from LPLV if schedule not fixed)
		Final Report (8 months from LPLV if schedule not fixed)
		Drug Manufacturing Complete

: Status 0 - complete through CSR
: Status 1 - ongoing study
: Status 2 - approved by Development Steering Committee (DSC)
: Status 3 - further discussion in Project Team is required

Attachment 2

List of the Benchmarks (calendar days)

Sep 29, 2014 updated version

Items	Target	Record in Akros	Comments
C-Stage Up to initial IND submission	**147**	120	JTE-151 IND submission in 120 days was Akros record. The target is set as 90% of the average in between 2009-2014.
Initial IND to First Dose	**44**	42	The target is set as 90% of the average in between 2009-2014.
Final PRT to First Dose <Ph1>	**49**	28	Former target based on 2003-2009 is kept as is. Average between 2009-2014 is 58.2
Final PRT to First Dose <Ph2>	**63**	49	Former target based on JTT-654 and JTT-130 phase 2 studies is kept as is. JTT-851 phase 2 was 91 days.
Ph1b Topline to Final Ph2a Protocol Synopsis	**46**	42	The target is 110% of Akros record (JTT-130). For JTT- 851, it was 81 days.
First draft PRT synopsis review meeting to Final Protocol	**46**	-	Former target based on JTT-851, JTZ-951 and JTE-051 first study is kept as is. Average of protocol synopsis finalization to final protocol between 2009-2014 is 46 days.
First to Last Randomization <Ph2>	**83** (under 200)	75 (654Ph2)	The target is 110% of Akros record. But complexity and difficulty of the study should be considered for this item. It was 93 days for JTT-851 Ph2 (301 subjects) and 129 days in JTT-130 Ph2(200< subjects).
	112 (201- 500)	93(851Ph2)	
Last observation to Source Data Verification	**7** <Ph1>	1	The target is determined by our experience. This item depends on action of clinical operation.
	14 <Ph2>	14	
Source Data Verification to Database Lock	**7** <Ph1>	2	The target is determined by our experience. This item consists of two parts; 1. SDV to Data cleaning (ready for PI sign-off) (CDM-related part) 2. Data cleaning to PI sign-off/Database lock (CLO-related part)
	16 <Ph2>	26	
Last observation to Database Lock	**14** <Ph1>	3	Average of recent cases after 2009 shows approximately 20 days for Ph1 and 48 days for Ph2. JTT-851 Ph2 was 40 days as Akros record.
	30 <Ph2>	40	
DB Lock to Topline	**14**	10	The target is the same as 2008 version.
DB Lock to CSR(body)	**120**	95	This target date is flexible, since a finalized CSR doesn't have any direct impact on other clinical activities. We will keep the former benchmark as is, but we will consider the task of CSR preparation more flexibly depending on the workload situation.
Ph1 Single dose start to Topline of multiple dose study	**11 months**	10 months	JTT-654 Ph1s were 10 months. Former target based on 2003-2009 experiences is kept as is. Average of the recent cases after 2009, JTE-151, JTZ-951 and JTK-853 was 347 days and supports the target.