Akros Clinical Development Goal 2014

Feb.3,2014

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. **Plan and/or undertake any additional ad-hoc studies in accordance with the updated development strategy.**

B. JTZ-951

1. **Complete LPLV of Phase 1 MAD HD-CKD (12-004) study by 2Q 2014. Complete Cohort 3 (10 mg) by the end of May at least.**
2. **Complete research task for Ph2 and establish the development plan in the US by 2Q 2014 and start preparation activities for Ph2 studies according to the updated strategy of the project.**

C. JTE-051

1. **Submit amendment for Ph1 MAD (13-002) study in 1Q 2014.**
2. **Prepare DDI studies for CYP and MTX and initiate them in 2Q 2014. Complete topline results in 3Q 2014.**
3. **Prepare JP population bridging study and initiate them in 3Q 2014. Complete topline results in 4Q 2014.**
4. **Prepare Ph2 study for RA and initiate it in 4Q 2014.**
5. **Start preparation activities of Ph2 study for 2nd indication according to the updated strategy of the project.**

D. JTE-151

1. **Complete topline results of Ph1 MAD (13-002) study by 2Q 2014.**
2. **Prepare DDI study for CYP and initiate it in 2Q 2014. Complete topline results in 3Q 2014.**
3. **Prepare JP population bridging study and initiate it by 4Q 2014.**
4. **Prepare P2 study for PS and initiate it in 4Q 2014.**

E. JTT-251

1. **Submit IND in Feb 2014. Initiate SAD study in 2Q 2014 and MAD study in 4Q 2014. Complete topline results of SAD study in 4Q 2014.**
2. **Discuss PoP study plan and fix it. According to the plan, prepare and start it.**

F. JTT-252

1. **Submit IND in Mar 2014. Initiate SAD study in 2Q 2014 and MAD study in 4Q 2014**

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, CSV Project Team, and Safety Review Committee activities to support clinical studies in Akros.**

2. **The following task force activities are planned in 2014.**

- **Organize and facilitate QA/QC consultation (D. Capano)**
  QA/QC consultation will be performed as needed in 2014to support Akros clinical development activities

- **Conversion of CSR to eCTD Format (A.Bastien/T. Ghaderi)**
  FDA accepts CSR in legacy format at this time. The goal is to convert CSR (clinical study report) in eCTD format for future submissions.

- **Akros Data Acquisition and Reporting Standards (K. Pu/A.Bastien/S.Light)**
  This document includes several components, some of which have been finalized. The goal is to finalize the remaining parts of ADARS and corroborate with JT team. (Section 2 should be done by Clinical Research)

- **Renew EDC enterprise contract for Medidata (S. Light/Terry/Masaki)**
  Team has already renewed the contract to be used Rave system by JT and Akros under a common contract. This year team will continue discussion to change the structure of contract including main signer.

- **Global eCRF Task Force (S. Light)**
  Task force will work forward a global eCRF and database shared by Akros and JT. The goal is to work efficiently with JT to reach agreement.

- **Integrated collaboration with Clinical Pharma, DMPK, and Tox groups in JT (S. Pai)**
  To identify topic(s) to be discussed and execute a meeting for more collaborative and efficient work.

- **DSUR Preparation (T. Ghaderi/G.Turcanu)**
  Team has already completed temple preparation in 2013. Task force will focus on creating the procedures and guidelines for DSUR preparation and on creating a blank template for DSUR.

- **Enhance KOL, Consultant network for Akros projects (A.Bastien/Masaki/Others)**
  To create better clinical study protocol or to consider a clinical development plan, input from KOL or consultants is needed. CLR group will create a data base of KOL/consultant contact information and useful panel for Akros.

- **Global study preparation Task Force(Masaki/Others)**
  Activities to prepare future global studies between JT and Akros will be initiated. Kick off meeting will be held and action plan will be discussed this year. Appropriate members will be considered in a step wise manner.

- **Improvement of tools and processes for safety and efficacy data review((A.Bastien/S.Light)**
  This TF will improve tools and processes that will allow for more effective and faster review of efficacy and safety data across programs as well as individual studies. This is the first year for the TF and the TF will set the goal and action plan for this year and future.

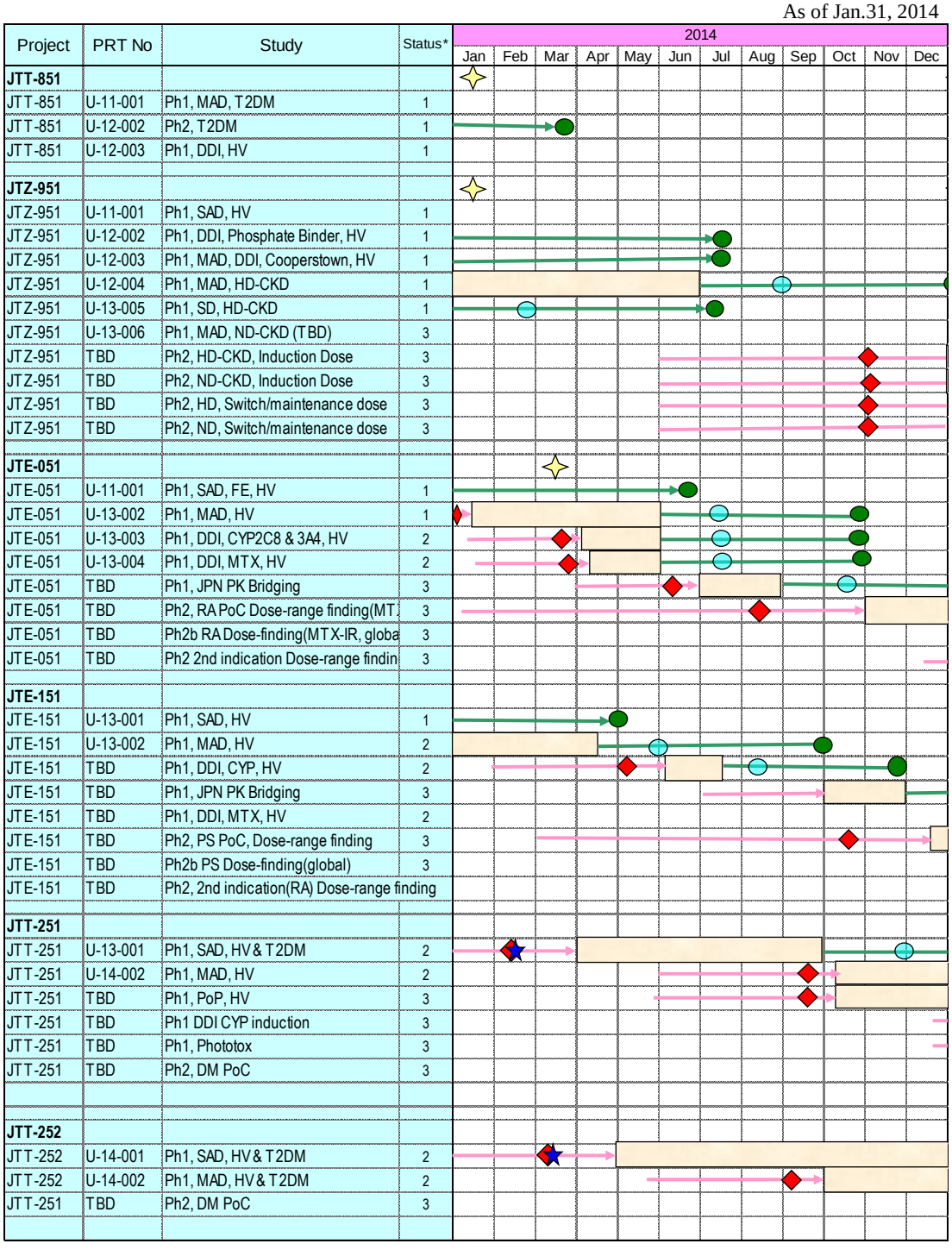
- **Task force to standardize responsibilities and workflow for clinical study-related deliverables (A.Bastien/Others)**
  Goal of this task force across departments at Akros is to create better collaboration across departments and to standardize responsibilities and workflow for certain deliverables (I.e. IB, protocol development, CSR).

- **Develop an electronic Trial Master File system using the Akros Documentum platform (D. Capano)**

Attachment 1
Akros Study Plan in 2014

As of Jan.31, 2014

Project	PRT No	Study	Status*
JTT-851			
JTT-851	U-11-001	Ph1, MAD, T2DM	1
JTT-851	U-12-002	Ph2, T2DM	1
JTT-851	U-12-003	Ph1, DDI, HV	1
JTZ-951			
JTZ-951	U-11-001	Ph1, SAD, HV	1
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-CKD, Induction Dose	3
JTZ-951	TBD	Ph2, ND-CKD, Induction Dose	3
JTZ-951	TBD	Ph2, HD, Switch/maintenance dose	3
JTZ-951	TBD	Ph2, ND, Switch/maintenance dose	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-13-003	Ph1, DDI, CYP2C8 & 3A4, HV	2
JTE-051	U-13-004	Ph1, DDI, MTX, HV	2
JTE-051	TBD	Ph1, JPN PK Bridging	3
JTE-051	TBD	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	2
JTE-151	TBD	Ph1, DDI, CYP, HV	2
JTE-151	TBD	Ph1, JPN PK Bridging	3
JTE-151	TBD	Ph1, DDI, MTX, HV	2
JTE-151	TBD	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	2
JTT-251	U-14-002	Ph1, MAD, HV	2
JTT-251	TBD	Ph1, PoP, HV	3
JTT-251	TBD	Ph1 DDI CYP induction	3
JTT-251	TBD	Ph1, Phototox	3
JTT-251	TBD	Ph2, DM PoC	3
JTT-252			
JTT-252	U-14-001	Ph1, SAD, HV & T2DM	2
JTT-252	U-14-002	Ph1, MAD, HV & T2DM	2
JTT-251	TBD	Ph2, DM PoC	3



Legend
- IND (CTA) Submission
- Annual Report or Drug Safety Report
- Study Preparation (IND, Protocol/IDB, Site Start-up)
- Final Protocol (4 months preparation time if schedule not fixed)
- 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

* Note
- : 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) As of Jan.31, 2014

Items	Target	Record in Akros	Comments
C-Stage Up to initial IND submission	**160**	146	JTK-853 IND was 146 days.
Initial IND to First Dose	**48**	42	The target is set as 90% of the average in between 2003-2009.
Final PRT to First Dose <Ph1>	**45**	28	The target is set as 90% of the average in between 2003-2009.
Final PRT to First Dose <Ph2>	**60**	49	The target is the average of JTT-654 and JTT-130 phase 2 studies in 2009.
Ph1b Topline to Final Ph2a Protocol Synopsis	**46**	42	The target is 110% of the Akros record.
First draft PRT synopsis review meeting to Final Protocol	**46**	-	The target was average of JTT-851, JTZ-951, and JTE-051 first study in Akros.
First to Last Randomization <Ph2>	**83** (under 200)	75 (654Ph2)	The target is 110% of the Akros record.
	142 (201- 500)	129(130Ph2)	
Last Visit to Source Data Verification	**14** <Ph1>		The target is determined based on our experience.
	28 <Ph2>		
Source Data Verification to Database Lock	**14** <Ph1>	27	The target is determined based on our experience.
	25 <Ph2>		
Last Visit to Database Lock	**28** <Ph1>	23	The target is determined based on our experience. The days in the record column were JTK-853 POC and JTT-130 PROMOTE.
	53 <Ph2>	56	
DB Lock to Topline	**14**	10	The target was the same as 2008 version.
DB Lock to CSR(body)	**(120)**	95	This target date is flexible, since finalized CSR doesn't have any direct impact to others. Especially, there are several remaining CSRs to be finalized for the studies conducted in 2013 and therefore we will consider the task of CSR preparation more flexibly depending on the work load situation in 2014.
Ph1 Single dose start to Topline of multiple dose study	**11 months**	10 months	JTT-654 Ph1s were 10 months.

*This benchmark is kept as is for the goal in 2013, but some changes might be added after ongoing updated analysis for recent study outputs. In the case of change, new target will be shared with the rationale.