FLASH NOTE

Company Update

USA | Healthcare | Biotechnology

December 15, 2014

Jefferies

Dicerna Pharmaceuticals (DRNA)

R&D Update: Positive DCR-PH1 Animal Data And Phase 1 Plans

BUY
Price target $48.00
Price $13.08

EQUITY RESEARCH AMERICAS

Key Takeaway

Today, DRNA provided an update of the ongoing development of its PH1 and pipeline programs. Notably, the company provided additional animal data for DCR-PH1 as well as an overview of its expected Phase 1 program, anticipated to begin in 2015 with initial data by YE15. The company also revealed early data from its DsiRNA-EX-conjugate platform, which will serve as the foundation for future liver-targeted programs.

DRNA Presents New Preclinical Data For DCR-PH1 That Suggest Robust, Durable Activity. DRNA presented new non-human primate (monkey) data, which showed robust and durable HAO1 knockdown following a single dose of DCR-PH1. Specifically, following a 0.3mg/kg dose of DCR-PH1 in mice, the company showed an average 93% knockdown of HAO1 at Day 1 and an average 54% knockdown at Day 28. For monkeys, there was an average knockdown of 84% at Day 4 and 68% at Day 29. The investigators showed that repeat dosing of 0.3mg/kg or 0.03mg/kg DCR-PH1 once every other week in mice led to significant sustained reductions of HAO1 mRNA. These findings were further supported by western blots and immunohistochemistry looking at the glycolate oxidase protein, which is encoded by the gene. These improvements in lab finding were borne out in the Mouse Ph1 model (AGXT-/-), in which repeat dosing with 0.3 mg/kg DCR-PH1 led to near normal levels of urinary oxalate. Kidney tissue samples showed that, compared to a placebo solution, mice treated with 0.3mg/kg had fewer calcium oxalate crystals in their kidneys after oral ethylene glycol challenges, an effect that was more pronounced, if they were treated earlier in the course of challenges. Overall, we see newly presented preclinical data as supportive of the potential efficacy DCR-PH1 may have in the treatment of PH1. Further, we are reassured by the durability of the response seen in preclinical models, as the company believes this could enable dosing frequency of once monthly in humans, a key benefit for chronic patient treatment.

DCR-PH1 Phase 1 Trial To Begin In 2015. DRNA expects to run a two-part, Phase 1/2 study beginning with a single ascending dose (SAD) trial followed by a multiple ascending dose (MAD) portion in PH1 patients who are not on dialysis. The SAD dose portion will enroll cohorts of 1-3 patients with PH1 to determine safety, PK, and PD (oxalate and glyolate levels). The MAD portion will enroll cohorts of 3-6 patients and will dose patients for three months, followed by an optional open-label extension period. Both trials will dose drug via an IV infusion over 30-60 minutes. The study is expected to begin in 2H15, with initial data from the SAD portion by YE15 and MAD data in 2016. Notably, the company estimated that HAO1 knockdown of at least 75% is their goal. Further, the company expects to start a natural history study in 1Q15 that will enroll 50-75 patients in the US and EU. The study will exclude patients on dialysis and will measure the change in oxalate and glycolate levels (urine and blood) as well as measures of clinical benefit including renal function.

Data For Proprietary Extended Dicer Substrate And Delivery Technology. DRNA has developed a proprietary DsiRNA-EX conjugate-based subcutaneous delivery system that will be used in lieu of Tekmira's LNP and DRNA's EnCore LNP in DRNA's pipeline of four new liver-targeted RNAi candidates. This delivery system allows for subcutaneously delivery. Today, the company provided early data showing equivalent potency between DsiRNA and DsiRNA-EX at a dose of 2 mg/kg as well as a suppressed immunostimulatory effect which may lead to decrease immunotoxicity. This dose would allow for convenient, small volume subcutaneous delivery in humans. DRNA also showed data from a mouse demonstrating silencing of a therapeutic liver target after a single subcutaneous injection of a DsiRNA-EX-conjugate. The company expects to provide additional details about this platform in 2015.

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Company Description

Dicerna Pharmaceuticals is a Watertown, MA-based therapeutics company focused on developing RNA interference (RNAi) technologies targeting liver and cancer. Dicerna has partnered two oncology development programs with the global pharmaceutical company Kyowa Hakko Kirin Co., Ltd. (KHK) targeting KRAS and CKAP5. DRNA's unpartnered programs are DCR-PH1 for Type 1 primary hyperoxaluria, a rare orphan disease resulting in renal failure, and DCR-M1711 targeting MYC for solid tumors.

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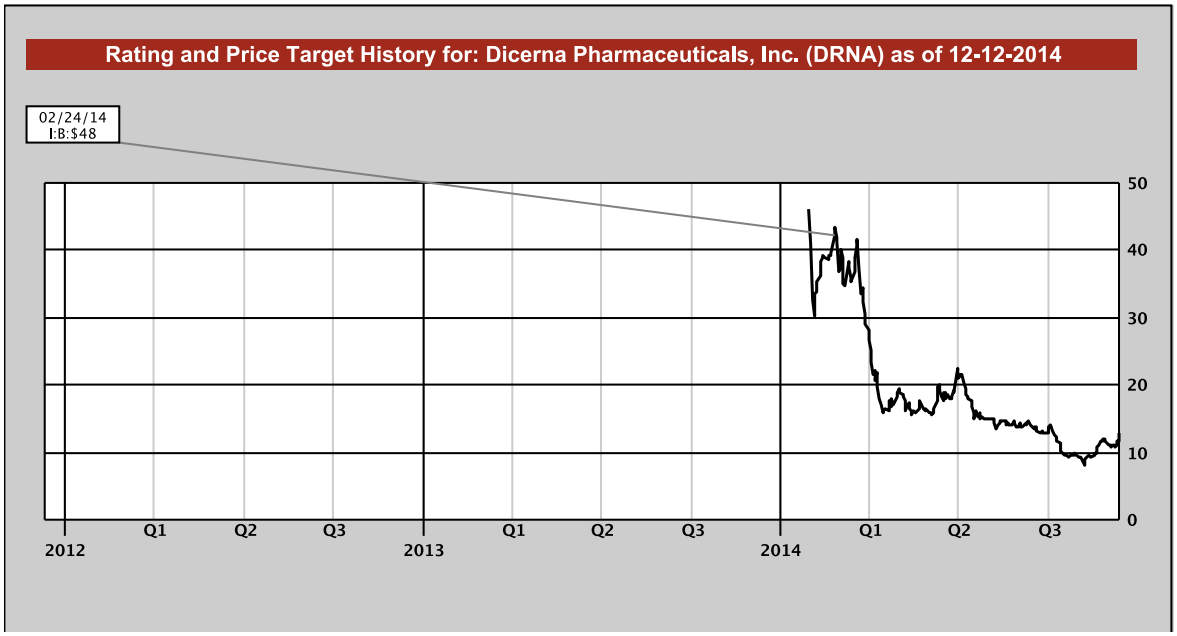

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