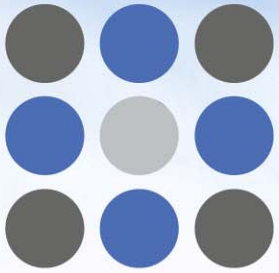


REATA

Conference Call on Bardoxolone Methyl in Alport Syndrome

November 14th, 2016

Development Path for Bardoxolone Methyl in Alport Syndrome

- In August 2016, Reata sought guidance from the FDA on a Phase 2 program in chronic kidney disease (CKD) caused by Alport syndrome
- Alport syndrome is a rare form of severe CKD with no approved therapy
- In October 2016, the FDA proposed a more efficient path to approval, recommending Reata run a single, pivotal trial
- FDA provided guidance that change in estimated glomerular filtration rate (eGFR) would support registration
  - Did not require a time to dialysis or transplant endpoint (ESRD)
  - Accelerated approval would be supported by a retained improvement in eGFR following 48 weeks of treatment and 4 weeks off drug
  - Full approval would be supported by a retained improvement in eGFR following 2 years of treatment and 4 weeks off drug
- Open-label Phase 2 portion of integrated Phase 2/3 trial will begin enrolling in 1H17

Bardoxolone Methyl (Bard) Overview

- **Bard promotes resolution of chronic inflammation by restoring mitochondrial function and has many potential applications**
  - Bard targets Nrf2 and promotes normal mitochondrial function, reducing ROS-mediated activation of NF-kB, the inflammasome, and pro-fibrotic pathways
  - In many diseases, these pathways are chronically activated
  - Bard has been tested in more than 2,000 patients
- **Reata is focused on rare, life-threatening diseases with few or no therapies**
  - During October, Reata initiated CATALYST, a Phase 3 trial in patients with pulmonary arterial hypertension from scleroderma and lupus (CTD-PAH)
  - Four Phase 2 trials underway in patients with pulmonary hypertension from interstitial lung disease
  - Three Phase 2 trials with omaveloxolone in Friedreich's ataxia, mitochondrial myopathies, and immuno-oncology are underway
- **Now initiating development program in Alport syndrome**

Bardoxolone Methyl (Bard) Overview

- **Recent CKD data from KHK created opportunity to utilize tractable endpoint in an orphan renal disease**
  - KHK is conducting Phase 2 study in patients with diabetic CKD
  - KHK reported Bard definitively improves “measured” GFR
- **KHK data validates improvements in eGFR observed in 6 prior Reata diabetic CKD studies with Bard**
  - Diabetic CKD studies showed improvements in eGFR, creatinine clearance, uremic solutes, and renal SAEs and ESRD events
  - BEACON Phase 3 stopped early due to unexpected fluid retention in a subset of patients
    - Later discovered only patients with advanced CKD, history of heart failure, and in or near active heart failure at baseline were at risk
    - Occurred only in first four weeks and could be monitored and treated
    - No fluid retention risk observed in subsequent studies
  - Cleared by FDA to conduct Phase 3 in CTD-PAH after review of safety data
- **Reviewed prior diabetic CKD data with FDA and sought guidance on Alport syndrome development program**

Alport Syndrome: A Brief Summary

- **Alport Syndrome Pathophysiology**
  - Mutations in type IV collagen cause defective glomerular filtration barrier
  - Patients usually present with hematuria, and then develop proteinuria and deterioration of kidney function, leading to ESRD
  - Due to loss of type IV collagen, deafness and ocular abnormalities also common
  - Like diabetic CKD, inflammation in the kidney promotes renal function loss
- **Patient Statistics**
  - Approximately 12,000 patients in the US and 40,000 globally
  - Median age at initiation of ESRD for males with most common form is 25
  - Median survival of approximately 55 years
- **Current Disease Management**
  - No approved therapies
  - ACE inhibitors and ARBs are commonly used
  - Dialysis or renal transplant is needed in most patients

Bard and Analogs Active in Animal Models Relevant to Renal Disease

- **Bard and analogs improve renal function and have anti-inflammatory and anti-fibrotic effects in many models of renal disease including protein overload models**

Model	General Findings
Protein Overload CKD *Zoja et al., ASN (2010)*	• Reduced oxidative/nitrosative stress, interstitial inflammation, and fibrogenic mediators including TGF-β and α-SMA • Decreased proteinuria and tubular damage
Ang II-Induced GFR Decline *Ding et al., Kidney Int (2014)*	• Increased inulin clearance by increasing K_f without affecting BP or renal plasma flow • Reduced whole glomeruli and mesangial cell contraction due to angiotensin II
5/6 Nephrectomy *Aminzadeh et al., Redox Biol (2013)*	• Reversed endothelial dysfunction and impaired Nrf2 activity in arterial tissue • Suppressed renal inflammation, injury, and infiltration of lymphocytes and macrophages • Mitigated systolic blood pressure increase caused by chronic renal failure
12-Month Monkey Safety Study *Reisman et al., J Am Soc Nephrol (2012)*	• Improved kidney function for 12-months without adverse renal histological effects • Induced renal Nrf2 targets and suppressed megalin
High Fat Diet-Induced CKD *Camer et al., Chem Biol Interact (2016)*	• Prevented HF diet-induced development of structural changes in the heart and kidneys • Prevented HF diet-induced renal corpuscle hypertrophy
Lupus Nephritis *Wu et al., Arthritis Rheumatol (2014)*	• Attenuated renal disease and reduced glomerulonephritis in three different models • Decreased proteinuria and BUN
Ischemic-Reperfusion *Wu et al, AJP Renal Physiol (2011)*	• Prevented structural injury from ischemia AKI • Pre-treatment preserved renal function following ischemic surgery
FeNTA-Induced Acute Kidney Injury *Tanaka et al, Tox Appl Pharm (2008)*	• Prevented acute kidney injury and preserved renal function • Reduced severity of proximal tubule degeneration and necrosis
Cisplatin-Induced Acute Kidney Injury *Aleksunes et al., JPET(2010)*	• Protected against cisplatin-induced renal toxicity • Reduced proximal tubule degeneration, apoptosis, necrosis, and inflammation

Bard has Consistently Improved Renal Function in Numerous Clinical Trials

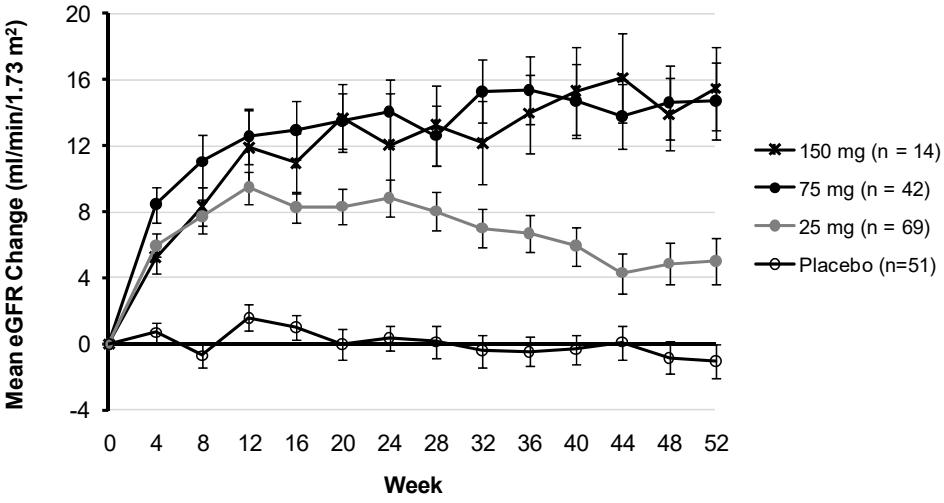
- **Bard significantly increases eGFR, inulin clearance, creatinine clearance, and other markers of renal function across 10 clinical trials that enrolled over 2,800 patients**

Study	Phase/ Country	Patient Population	N	ΔeGFR (mL/min/1.73m²)
402-C-0903 **(BEACON)**	3/Global	CKD/Diabetes	2185	6.4 (p<0.001 vs PBO)
402-C-0804 **(BEAM)**	2/US	CKD/Diabetes	227	8.6 (p<0.001 vs PBO)
RTA402-005 **(TSUBAKI)**	2/Japan	CKD/Diabetes	40	Data not yet publicly disclosed
402-C-0902	2/US	CKD/Diabetes	131	6.5 (p<0.001)
402-C-0801 (Stratum 1)	2a/US	CKD/Diabetes	60	6.7 (p<0.001)
402-C-0801 (Stratum 2)	2b/US	CKD/Diabetes	20	7.2 (p<0.001)
402-C-1102	1/US	CKD/Diabetes	24	9.0 (p<0.05)
402-C-0501	1/US	Cancer	47	18.2 (p<0.0001)
402-C-0702	1/2/US	Cancer	34	32.2 (p=0.001)
402-C-1302 **(LARIAT)**	2/US	Pulmonary Hypertension	54	14.7 (p<0.001 vs PBO)

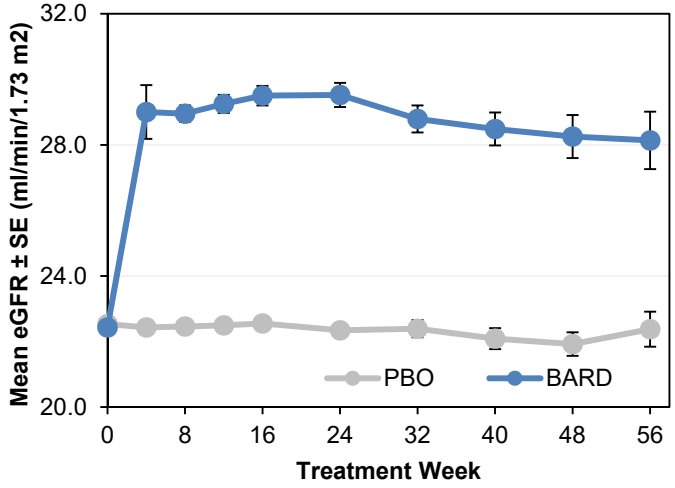
Patients with Chronic Kidney Disease and Type 2 Diabetes Show Significant Renal Function Improvement

- Bard significantly increased eGFR (p<0.0001) in BEAM and BEACON
- Change was durable through one year, the longest duration tested
- Changes were associated with fewer renal SAEs and ESRD events

BEAM



BEACON



Number of Patients

PBO	1093	1023	885	726	547	402	281	125
BARD	1092	958	795	628	461	345	241	103

Pergola et al., NEJM (2011); De Zeeuw et al., NEJM (2013)

Bard Improves Kidney Function Post-Withdrawal

- In BEAM and BEACON, significant placebo-corrected improvement in eGFR 4 weeks after drug withdrawal
  - eGFR assessed after sub-therapeutic concentrations reached
  - End-of-treatment and withdrawal eGFR changes correlate
  - The larger the effect on-treatment, the larger the retained effect
  - Data suggest Bard affects chronic remodeling and fibrosis

Withdrawal Analysis

	Baseline eGFR	Placebo-Corrected ΔeGFR Post-Withdrawal	P-value
BEAM (n=172)			
Low Dose	33	0.6	p>0.05
Mid Dose	32	4.7	p<0.05
High Dose	32	5.0	p<0.05
BEACON (n=498)			
20 mg	23	1.8	p<0.001

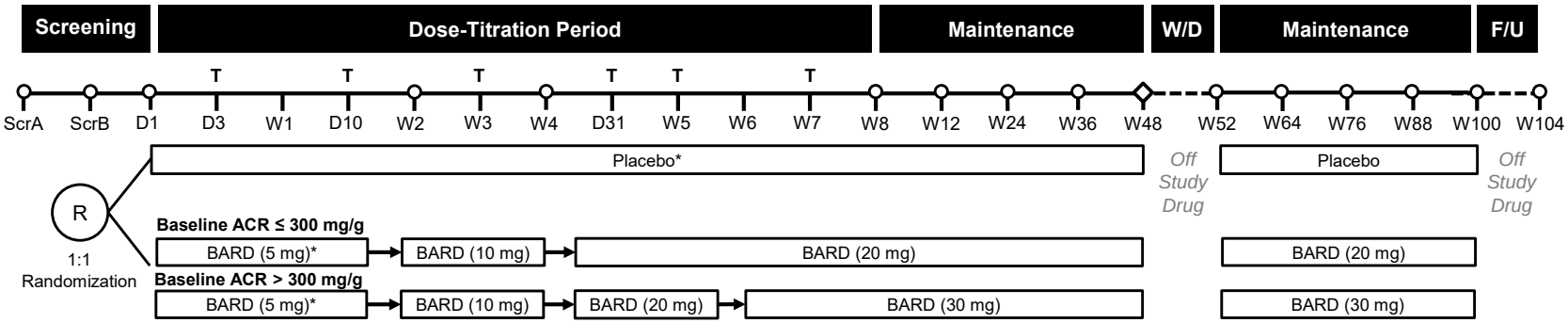
Phase 2/3 Trial Design

- **Have designed the trial in collaboration with international key opinion leaders and the Alport Syndrome Foundation**
  - **Will enroll patients from 12 to 60 years old**
  - **Will enroll a broad range of kidney function (eGFR between 30-90 mL/min/1.73 m^2; stage 4 patients excluded)**
  - **Patients with cardiovascular disease or fluid retention will be excluded**
- **Phase 2 Cohort**
  - **Open-label cohort enrolling a total of 30 patients**
    - **15 with microalbuminuria**
    - **15 with macroalbuminuria**
  - **Will measure change in eGFR following 12 weeks of treatment**
  - **Following analysis at 12 weeks, patients will remain on treatment for two years**
  - **Data not included in analysis of primary and secondary endpoints for Phase 3**
  - **Enrollment expected to begin 1H17**
- **Phase 3 Cohort**
  - **Will enroll up to 180 patients with two years of follow-up**
  - **Placebo-controlled, double-blind trial with 1:1 randomization**

Phase 2/3 Trial Design

- Titration to be used to reach goal dose of 20 or 30 mg given orally, once daily
- Endpoints for Accelerated and Full Approval
  - Primary endpoint of on-treatment eGFR change at Week 48
  - Key Secondary endpoint of eGFR change after 4 weeks of drug withdrawal (Week 52)
  - Additional secondary endpoints of eGFR change at Week 100 and after 4 weeks of drug withdrawal (Week 104)
  - Significant and robust effect on primary and key secondary endpoint (Week 52) could serve as the basis for accelerated approval
  - Continued effect at Week 104 could serve as the basis for full approval

Phase 3 Cohort



Data From Previous Trials

- **Design leverages data from 2,600 CKD patients and 400 treated for 48 weeks**
  - Withdrawal change predicted by on-treatment change
  - On-treatment change is predicted by baseline eGFR, baseline ACR and drug exposure
- **Monitoring and dose titration to minimize risk of adverse events**
  - Both approaches have worked well in partner's ongoing diabetic CKD trial
  - Titration has minimized adverse events and drop-outs in our trials (PAH/PH-ILD)
  - Careful monitoring after randomization allows for early intervention
- **99% and 90% power to achieve primary and secondary endpoints**
  - Goal is to replicate BEAM (4.7 mL/min/1.73 m^2 difference) with twice as many patients
  - Study could be successful with effect that is approximately 50% less than BEAM

	N	BL eGFR	Placebo-Corrected ∆eGFR		
			Week 12	One Year	Withdrawal
BEAM: Mid Dose	90	32.3	12	16 (p<0.001)	4.7 (p=0.02)
CARDINAL Modeling					
Replicate BEAM with more patients	180	60	12	16 (p<0.001)	4.7 (p<0.001)
Minimal detectable difference					2.5 (p<0.05)

Upcoming Key Events and Timing

Program	Indication	Event	Timing
Bardoxolone methyl	Alport syndrome	Phase 2/3 Initiation	1H 2017
	PH-ILD-CTD	Phase 2 Top-line Data	2H 2017
	PH-ILD-IPF	Phase 2 Top-line Data	2H 2017
	PH-NSIP	Phase 2 Top-line Data	2H 2017
	PH-SARC	Phase 2 Top-line Data	2H 2017
	CTD-PAH	CATALYST Phase 3 Top-line Data	1H 2018
Omaveloxolone	Friedreich's ataxia	Phase 2 Top-line Data (Part 1)	1H 2017
	Mitochondrial Myopathies	Phase 2 Top-line Data (Part 1)	1H 2017
	Immuno-Oncology	Phase 1b Data	2H 2017