**METHODS:** Patients could enter PATENT-2 after successful completion of PATENT-1 and if they were without any ongoing riociguat-related serious adverse events. During the initial 8-week blinded period of PATENT-2, patients originally randomized to the riociguat 2.5 mg–maximum group continued on their optimum dose (up to 2.5 mg three times daily [tid]) while receiving sham dose adjustment; patients originally randomized to placebo or riociguat 1.5 mg–maximum (up to 1.5 mg tid) were adjusted to their optimum dose (up to 2.5 mg tid). The primary endpoints were safety and tolerability; secondary endpoints included 6MWD and World Health Organization functional class (WHO FC).

**RESULTS:** Of the 443 patients in PATENT-1, 396 (89%) entered PATENT-2. In this interim analysis (cut-off March 2013), 324 (82%) patients were ongoing, and 334 (84%) had received ≥1 year of treatment. Overall, 8% of patients withdrew due to adverse events. Long-term riociguat was well tolerated, with no new safety signals. At the end of PATENT-1, 6MWD increased by +37±52 m (mean±SD) in the 2.5 mg–maximum group, +46±51 m in the 1.5 mg–maximum group, and +12±58 m in the placebo group of the cohort entering PATENT-2. After 1 year of PATENT-2 (overall cohort; n=327), 6MWD increased by +51±74 m versus PATENT-1 baseline. At the end of PATENT-1, WHO FC was improved/stabilized/worsened in 21/78/2%, 25/69/5%, and 16/74/9% (data missing for one patient) of patients in the 2.5 mg–maximum, 1.5 mg–maximum, and placebo groups, respectively. After 1 year (overall cohort; n=339), the proportion of patients with improved/stabilized/worsened WHO FC was 33/61/6%. At 1 year, 54% of ongoing patients were receiving combination therapy; 97% of pre-treated patients remained on combination therapy and 3% had transitioned to riociguat monotherapy, while 11% of treatment-naïve patients were receiving additional PAH medication.

**CONCLUSIONS:** Long-term riociguat is well tolerated in patients with PAH and shows sustained benefits in 6MWD and WHO FC when used as a monotherapy or in combination with concomitant PAH therapies. Therefore, riociguat is a promising option for the long-term treatment of patients with PAH.

**TYPE:** Clinical Science