patients and after treatment initiation for nusinersen-treated patients. **Results:** A total of 349 SMA1 patients (median age=1 year; 55.6% female) with median follow-up of 7.9 months were included. The proportion of patients receiving mechanical ventilation, nutritional support, and physical therapy/rehabilitation was 46.4%, 46.1%, and 22.6%. Patients had, on average, 59.4 days with medical visits/year (14.1 inpatient, 13.4 respiratory failure-related). The 45 nusinersen-treated patients had, on average, 56.6 days with medical visits/year (4.6 inpatient, 11.4 respiratory failure-related). Excluding nusinersen-related costs, mean healthcare costs PPPY were $137,627 (median: $43,167) for all patients and $92,618 ($29,425) for nusinersen-treated patients. Mean nusinersen-related costs were $191,909 ($144,487) per month for the first 3 months post-initiation and $36,882 ($16,132) per month thereafter. **Conclusions:** HRU and costs associated with SMA1 are substantial, even among patients treated with nusinersen.

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SUNFISH Part 1 results and Part 2 trial design in patients with type 2/3 spinal muscular atrophy (SMA) receiving risdiplam (RG7916)

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Background: SMA is characterized by reduced levels of survival of motor neuron (SMN) protein from deletions and/or mutations of the *SMN1* gene. While *SMN1* produces full-length SMN protein, a second gene, *SMN2*, produces low levels of functional SMN protein. Risdiplam (RG7916/RO7034067) is an investigational, orally administered, centrally and peripherally distributed small molecule that modulates pre-mRNA splicing of *SMN2* to increase SMN protein levels. **Methods:** SUNFISH (NCT02908685) is an ongoing multicenter, double-blind, placebo-controlled, operationally seamless study (randomized 2:1, risdiplam:placebo) in patients aged 2–25 years, with Type 2/3 SMA. Part 1 (n=51) assesses safety, tolerability, pharmacokinetics and pharmacodynamics of different risdiplam dose levels. Pivotal Part 2 (n=180) assesses safety and efficacy of the risdiplam dose level selected based on Part 1 results. **Results:** Part 1 results showed a sustained, >2-fold increase in median SMN protein versus baseline following 1 year of treatment. Adverse events were mostly mild, resolved despite ongoing treatment and reflected underlying disease. No drug-related safety findings have led to withdrawal (data-cut 06/17/18). SUNFISH Part 1 exploratory endpoint results and Part 2 study design will also be presented. **Conclusions:** To date, no drug-related safety findings have led to withdrawal. Risdiplam led to sustained increases in SMN protein levels.

P.064

FIREFISH Part 1: 1-year results on motor function in infants with Type 1 spinal muscular atrophy (SMA) receiving risdiplam (RG7916)

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Background: SMA is characterized by reduced levels of survival of motor neuron (SMN) protein from deletions and/or mutations of the *SMN1* gene. While *SMN1* produces full-length SMN protein, a second gene, *SMN2*, produces low levels of functional SMN protein. Risdiplam (RG7916/RO7034067) is an investigational, orally administered, centrally and peripherally distributed small molecule that modulates pre-mRNA splicing of *SMN2* to increase SMN protein levels. **Methods:** FIREFISH (NCT02913482) is an ongoing, multicenter, open-label operationally seamless study of risdiplam in infants aged 1–7 months with Type 1 SMA and two *SMN2* gene copies. Exploratory Part 1 (n=21) assesses the safety, tolerability, pharmacokinetics and pharmacodynamics of different risdiplam dose levels. Confirmatory Part 2 (n=40) is assessing the safety and efficacy of risdiplam. **Results:** In a Part 1 interim analysis (data-cut 09/07/18), 93% (13/14) of babies had ≥4-point improvement in CHOP-INTEND total score from baseline at Day 245, with a median change of 16 points. The number of infants meeting HINE-2 motor milestones (baseline to Day 245) increased. To date (data-cut 09/07/18), no drug-related safety findings have led to patient withdrawal. No significant ophthalmological findings have been observed. **Conclusions:** In FIREFISH Part 1, risdiplam improved motor function in infants with Type 1 SMA.

P.065

AVXS-101 gene-replacement therapy (GRT)) in presymptomatic spinal muscular atrophy (SMA): study update

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Background: SMA is a neurodegenerative disease caused by biallelic deletion/mutation of *SMN1*. Copies of a similar gene (*SMN2*) modify disease severity. In a phase 1 study, *SMN* GRT onasemnogene abeparvovec (AVXS-101) improved outcomes of symptomatic SMA patients with two *SMN2* copies (2x*SMN2*) dosed ≤6 months. Because motor neuron loss can be insidious and disease progression is rapid, early intervention is critical. This study evaluates AVXS-101 in presymptomatic SMA newborns. **Methods:** SPR1NT is a multicenter, open-label, phase 3 study enrolling ≥27 SMA patients with 2–3x*SMN2*. Asymptomatic infants ≤6 weeks receive a one-time intravenous AVXS-101 infusion ($1.1x10^{14}$ vg/kg). Safety and efficacy are