Background

- Spinal muscular atrophy (SMA) is a severe, progressive, inherited neuromuscular disease leading to loss of motor function and reduced life expectancy.1
- SMA is caused by reduced levels of the survival of motor neuron (SMN) protein due to deletions and/or mutations of the SMN1 gene.1,2
- A second SMN gene, SMN2, produces only low levels of functional SMN protein.2
- Increasing preclinical evidence indicates that SMA is a multisystem disease.2

- Risdiplam (RG7916) is an investigational, orally administered, centrally and peripherally distributed small molecule that modulates SMN2 pre-mRNA splicing to increase SMN protein levels.3

Study design

- JEWELFISH (NCT03023172) is a multicenter, open-label study primarily evaluating the safety and tolerability of once-daily oral administration of risdiplam in patients aged from 6 months to 60 years with SMA who have previously enrolled in Study BP29420 (MOONFISH) with the splicing modifier RO6885247 or received previous treatment with nusinersen, edasalonexocse or AVXS-101.1
- A proposed protocol amendment* will include patients who have received previous treatment with AVXS-101.

Patients in JEWELFISH show a diversity of copy number, SMA type and ambulatory status

<table>
<thead>
<tr>
<th>All patients (N=12)</th>
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<tr>
<td>Age at screening, years, median (range)</td>
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<tr>
<td>Gender, female/male, n (%)</td>
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<tr>
<td>Risdiplam treatment duration, median days (range)</td>
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<tr>
<td>SMA Type 2, n (%); Type 3, n (%)</td>
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<tr>
<td>SMN2 copy number, n (%)</td>
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<td>Previous therapy, n (%)</td>
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<td>Ambulatory, n (%)</td>
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<td>Non-ambulatory, n (%)</td>
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<td>MFM32 at baseline, median (range)</td>
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Data cut-off is July 2018, except-to-treat patients.

To date,* no drug-related safety findings have led to withdrawal

- Safety data is available from 12 patients exposed to risdiplam from 57–512 days:
  - ophthalmologic monitoring did not show any evidence of the retinal findings seen in preclinical monkey studies
  - 41 mild or moderate events were reported in 10 patients
  - the most frequent events were nasopharyngitis (3 events in 2 patients), pyrexia (3 events in 2 patients) and headache (3 events in 2 patients)
  - no serious AEs were reported; no adverse trends were reported after a review of all available safety laboratory results, vital signs and EQQ data

Abbreviations

- AEs, adverse events; AEUR, area under curve; C_out, trough plasma concentration; C_tmax, mean plasma concentration; C_max, peak plasma concentration; MFM, motor function measure; mRNA, messenger ribonucleic acid; PD, pharmacodynamics; PK, pharmacokinetics; Q, quarter; SMA, spinal muscular atrophy; SMN, survival of motor neuron.

Acknowledgments

We want to thank all patients and their families for their participation in these studies. This study is funded by F Hoffmann-La Roche AG, Basel, Switzerland. The authors thank Paul Grimsey of Roche Pharmaceutical Research and Early Development, Roche Innovation Center Basel, Basel, Switzerland for data analysis support. We would like to thank all investigators, site collaborators, PKs and sponsors for the study. The study was performed at the Roche Innovation Center Basel. The safety data were analyzed and statistics were done by Roche Innovation Center Basel. Data were managed using Meddronic R3, Roche’s own data management software, and were processed by Reckitt Benckiser at Meddronic. The study was sponsored by Roche Pharmaceuticals, Basel, Switzerland.

References

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