

Safety Profile of the Novel, Intra-articular Agent Lorecivivint (LOR; SM04690), a CLK/DYRK1A Inhibitor That Modulates the Wnt Pathway, in Subjects with Knee Osteoarthritis

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I authorize the recording and disclosure of my presentation at **22 Pan-American Congress of Rheumatology**

Disclosures

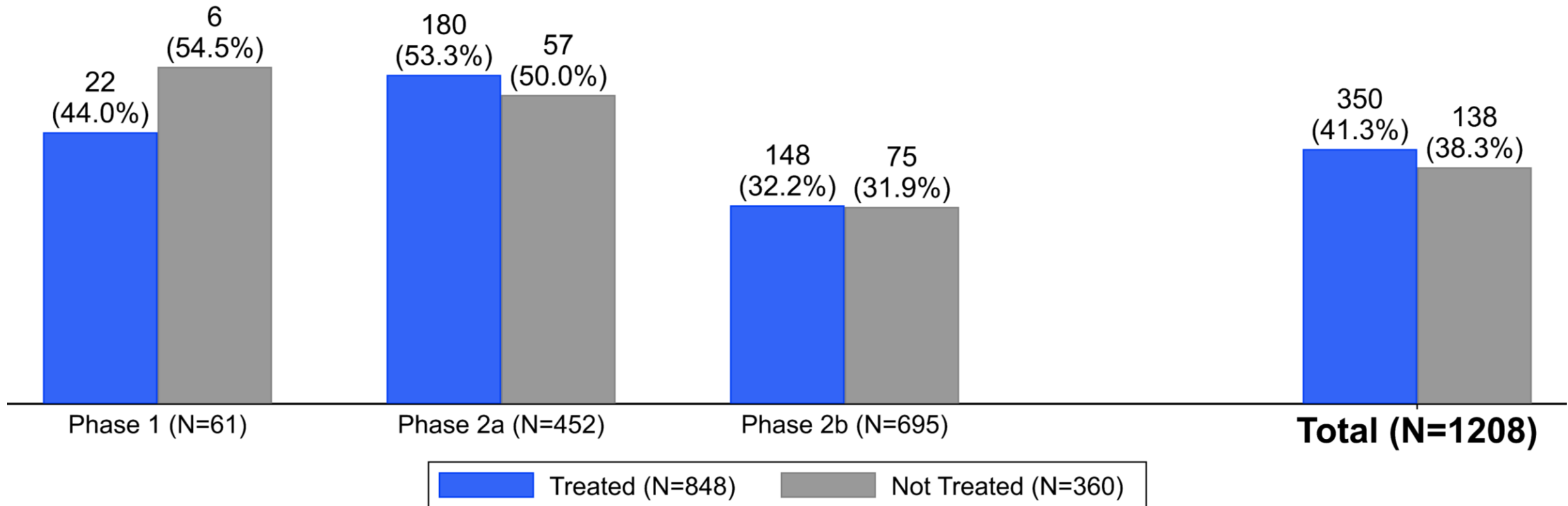
- **Ismail Simsek, MD:** Samumed employee and shareholder
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Background and methods

- Safety concerns regarding osteoarthritis (OA) pharmacotherapy have reinforced the unmet need for safe and effective OA therapies
- Lorecivivint (LOR), an intra-articular (IA) CLK/DYRK1A inhibitor that modulates the Wnt pathway,^{1,2} is in Phase 3 trials as a potential disease-modifying treatment for knee OA
- The safety profile of LOR to date was evaluated by a pooled analysis of 3 completed placebo-controlled trials (Phase 1, 2a, 2b)^{3–5}

1. Deshmukh V, et al. *Osteoarthritis Cartilage*. 2017.
2. Deshmukh V, et al. *Osteoarthritis Cartilage*. 2019.
3. <https://clinicaltrials.gov> (Identification No. NCT02095548).
4. <https://clinicaltrials.gov> (Identification No. NCT03122860).
5. <https://clinicaltrials.gov> (Identification No. NCT02536833).

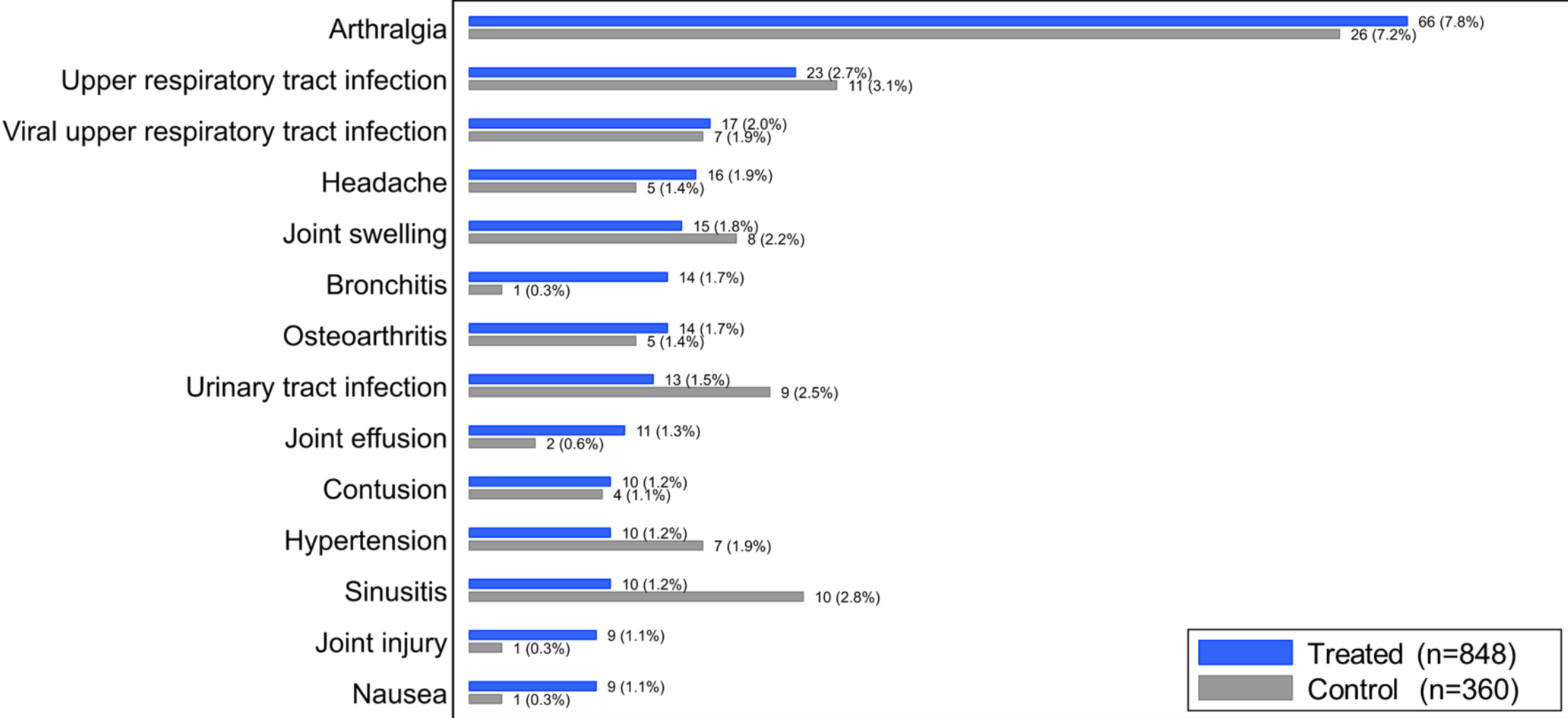
AE rate between control and active subjects consistent across studies and overall



*All subjects received intra-articular procedures.

Integrated safety summary: AEs reported in >1% of treated subjects

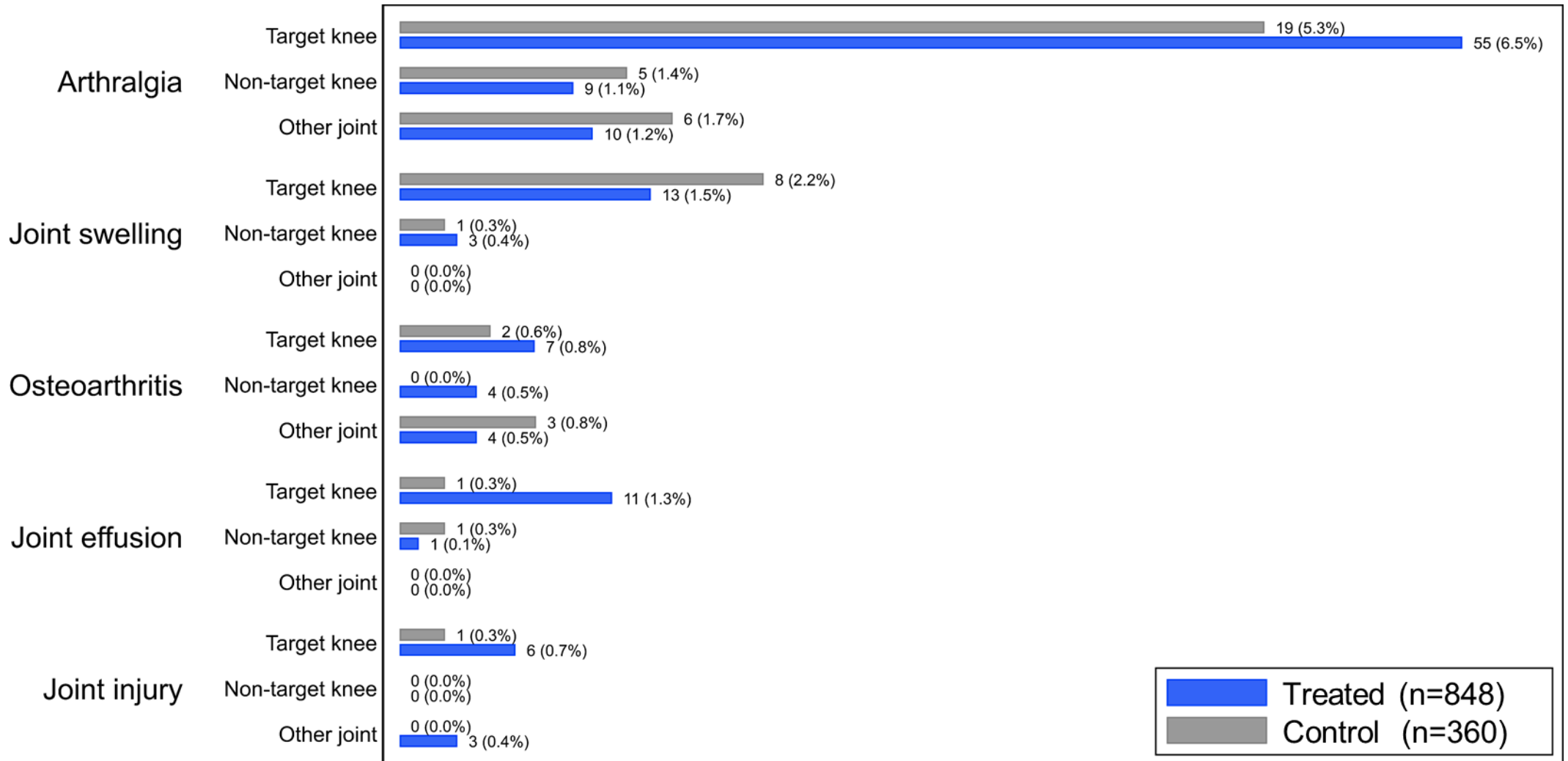
Total clinical trial population (N=1208)



Safety data from completed trials. All subjects received intra-articular injections.

Integrated safety summary: Joint-related AEs

Total clinical trial population (N=1208)



Safety data from completed trials. All subjects received intra-articular injections.

Integrated safety summary: Bone health-related AEs

Total clinical trial population (N=1208)

- 16 bone health-related AEs in 12/1208 (1.0%) subjects
 - 2 osteopenia/osteoporosis in 2 LOR-treated postmenopausal women
 - 14 fractures in 10 subjects (7 LOR-treated, 3 control)
 - 3 patellar (2 non-target knee, 1 target knee), 3 vertebral, 2 foot, 2 wrist, 2 rib, 1 fibula, 1 hand
- All fractures were adjudicated by the medical monitors and determined to be caused by trauma; all healed uneventfully within the expected time frame

Serious adverse event summary

From Safety Review: 2018-10-23	Lorecivivint (LOR)				
	0.03 mg (N=234)	0.07 mg (N=235)	0.23 mg (N=226)	All LOR* (N=801)	Placebo (N=353)
Total SAEs (%)	9 (3.8)	13 (5.6)	7 (3.1)	29 (3.5)	4 (1.1)
Cardiac Disorders	2 (0.8)	4 (1.6)	0 (0.0)	6 (0.7)	1 (0.3)
Infections	3 (1.2)	2 (0.8)	1 (0.4)	6 (0.7)	0 (0.0)
Renal / Urinary Disorders	1 (0.4)	1 (0.4)	1 (0.4)	3 (0.4)	0 (0.0)
Vascular Disorders	1 (0.4)	2 (0.8)	0 (0.0)	3 (0.4)	0 (0.0)
Injury / Procedural Complications	0 (0.0)	0 (0.0)	2 (0.8)	2 (0.2)	1 (0.3)
Neoplasms	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.2)	0 (0.0)
Reproductive System Disorders	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.2)	0 (0.0)
Congenital / Genetic Disorders	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)
Gastrointestinal Disorders	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Hepatobiliary Disorders	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)
General Disorders / Administration Site Condition	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.1)	0 (0.0)
Nervous System Disorders	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Musculoskeletal / Connective Tissue Disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Respiratory Disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

There were no deaths. All SAEs were deemed unrelated to LOR by investigator.

*The 0.15 mg LOR (N=106) group had no SAEs. Formulation errors not reported.

Conclusions

- Based on AEs observed in completed trials (N=1208), IA LOR for the treatment of painful knee OA appeared to be safe and well tolerated
- Individual AEs were reported at comparable rates between groups
- Incidence of bone health-related AEs was similar between groups
- No SAEs were deemed related to LOR by investigators
- Clinical development of LOR as a treatment for knee OA is ongoing

Thank you