Susan Macdonald[1], Valerie Cullen[1], Todd Brady[1], Isaac Levi[2], Sigal Meilin[2] and **Scott Young[1]**
[1]Aldeyra Therapeutics, USA
[2]MD Biosciences Inc., USA

A variety of aldehyde species have been shown to activate ion channels, such as TRPA1 and TRPV1, involved in mediatin pain. Furthermore, aldehyde dehydrogenase 2 which diminishes aldehyde loads by oxidizing aldehydes to acids has bee shown to modulate acute in ammatory pain in animal models. us, aldehyde signaling represents a novel therapeutic target for the treatment of pain. ADX-102 is a novel small molecule that covalently binds aldehydes including malondialdehyde and 4-hydroxynonenal, which have been shown to mediate in ammatory pain. For that reason, the e ect of ADX-102 on acute in ammatory pain was tested in the carrageenan-induced and Complete Freund's Adjuvant (CFA)-induced models in mice. ADX-102 was administered intraperitoneally prior to and a er pain induction, at di erent doses and schedules (30 mg/kg twice daily [BID], 100 mg/kg once daily [QD], or 100 mg/kg BID). ermal hypersensitivity, mechanical hypersensitivity and paw swelling were assessed at various times to explore the e ect of modulating aldehyde signaling on di erent molecula mechanisms underlying pain. Diclofenac was used as a positive control and vehicle was used as a negative control. ADX-1(mediated dose-dependent reductions in nociceptive behavior in both models of acute pain. In the CFA model, treatment with 100 mg/kg QD or 100 mg/kg BID ADX-102 resulted in statistically signi cant reductions in thermal hypersensitivity, but reduced mechanical hypersensitivity only a er treatment with 100 mg/kg ADX-102 BID. In the carrageenan model, ADX-102 treatment resulted in statistically signi cant reductions in thermal hypersensitivity at ADX-102 doses of 30 mg/kg BID and 100 mg/kg BID, but did not a ect mechanical hypersensitivity. Minor e ects on paw swelling were observed in both models. e data imply that ADX-102 may di erentially a ect thermal and mechanical pain pathways. Overall, the results support the role of aldehyde signaling in pain and suggest that aldehyde traps represent a novel approach for the treatment of pain.

Susan Macdonald received her PhD from the University of Massachusetts Medical School and did Post-doctoral work at Onyx Pharmaceuticals. She has extensive experience in Research and Development in the biopharmaceutical industry and is currently Vice President of Research and Development at Aldeyra Therapeutics, a biotechnology compD f.ayweloingl aproperitatryfamitly ofnalehydce andtchue hivebroade