

Aclaris's second crack at a topical Jak



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But, with Incyte close to market and several big players moving forward, Aclaris's project will need to stand out from the pack.

Aclaris's first attempt at developing a topical Jak inhibitor [did not make it past mid-stage testing](#), but the company's follow-on project, ATI-1777, looks to have better legs. Yesterday the company unveiled a statistically convincing win in a phase 2a atopic dermatitis trial, and plans to push into a larger study.

The data are notable considering the strong responses in the control cohort – which are not uncommon in these trials. But a placebo cream is probably the least of Aclaris's worries. Incyte looks set to receive approval for topical ruxolitinib later this month, and several big players, including Novartis and Leo Pharma, are moving forward with similar projects.

Leo, a private European dermatology player, recently started two large pivotal studies of its project delgocitinib in hand eczema, with atopic dermatitis in earlier stages of development in the west, so is perhaps not a direct competitor just yet.

Novartis and Pfizer are also still both in mid-stage trials. Pfizer's plans for brepocitinib, which also hits Tyk2, are not immediately clear. But Novartis's pan-Jak inhibitor CEE321 featured at the company's [R&D day 18 months ago](#), so the Swiss giant clearly has plans for the asset.

Incyte represents the biggest competition for now. The company already sells an oral formulation of ruxolitinib as Jakafi for myelofibrosis. The topical version is expected to be selling \$791m by 2026, according to *Evaluate Pharma's* sellside consensus – a respectable sum that suggests room for more than one player.

Here come the topical Jaks: leading contenders

Project	Company	Note	Mechanism
<i>Filed</i>			
INCB018424 (ruxolitinib)	Incyte	Pdufa data for atopic dermatitis 21 Jun 2021; to be filed in vitiligo H2 2021	Jak 1&2 inhibitor
<i>Phase 3</i>			
Delgocitinib	Leo Pharma (marketed in Japan for atopic dermatitis by Torii as Corectim; from Japan Tobacco)	Ph3 in chronic hand eczema	Jak inhibitor
<i>Phase 2</i>			
ARQ-252	Arcutis Biotherapeutics	Ph2 in chronic hand eczema failed Q1 2021; ph2a in vitiligo due to report H2 2023	Jak1 inhibitor
ATI-1777	Aclaris Therapeutics	Ph2a in atopic dermatitis successful Q2 2021; ph2b planned	Jak 1&3 inhibitor
DMVT-502 (erdulatinib)	Dermavant/Sinovant (from Portola)	Ph2 in vitiligo completed but no data reported; company states ph1 in atopic dermatitis but no trial listed	Jak & Syk inhibitor
PF-06700841 (brepocitinib)	Pfizer	Ph2 trials in atopic dermatitis/psoriasis completed, further plans unclear	Tyk2 & Jak1 inhibitor
<i>Phase 1</i>			
CEE321	Novartis	Ph1 in atopic dermatitis	Pan-Jak inhibitor
<i>Source: Evaluate Pharma & company statements.</i>			

The data released on ATI-1777 yesterday were in only 50 patients, but for an inkling of relative efficacy they can be compared - with the usual caution - to published phase 2 data on ruxolitinib. While the numbers below appear to show similar efficacy for the two projects, the picture shifts in ruxolitinib's favour when the data are placebo-adjusted.

These figures are from small trials, of course, and because ruxo was filed on data concerning entirely different endpoints it is hard to compare the larger phase 3 datasets with ATI-1777. The primary endpoint of ruxo's twin pivotal trials, True-AD1 and 2, was proportion of patients achieving investigator's global assessment of treatment success (IGA-TS), defined as an IGA score of 0 or 1 with improvement of at least two grades from baseline. Both trials hit the measure with significance.

Cross-trial comparison of Jaks in atopic dermatitis

Company	Incyte				Aclaris			
Jak	Ruxolitinib 0.15% QD to 1.5% BID				ATI-1777 2%			
Trial	Phase 2 (NCT03011892)				Phase 2: AD-201 (NCT04598269)			
N	307 (50 on 1.5% BID dose)				50			
Primary endpoint	% chg from baseline in EASI at 4wk				% chg from baseline in modified EASI at 4wk			
	Drug*	Vehicle	Difference	P value	Drug	Vehicle	Difference	P value (one-sided)
	71.6	15.5	56.1	<0.0001	74.4	41.4	33.0	<0.001
Application-site pain (%)	2.0	3.8			-	-		
Application site pruritus (%)	-	-			2.0	0.0		

*Data for 1.5% BID dose. Source: [Journal of Allergy and Clinical Immunology](#) & [company presentation](#).

Aclaris's data were apparently strong enough to support a fund raising: the company also announced a \$75m offering yesterday. And success with ATI-1777 adds a second viable asset to its pipeline, with investors more focused on ATI-450, [an oral rheumatoid arthritis project that impressed in January](#).

But the topical Jak space looks like it could be getting crowded. And, with big pharma eyeing the market, smaller groups like Aclaris and even Incyte must get approvals fast, and make the most of their advantage.

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