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Glaxo follows Jounce with an Icos setback



Glaxosmithkline's efforts to make progress in oncology have taken another knock with the discontinuation of two phase 3 trials of its Icos agonist feladilimab. The studies in question are in head and neck cancer in combination with Merck & Co's Keytruda: Induce-3 is in PD-L1-positive subjects, while Induce-4, in all-comers, additionally gives chemo. Two remaining phase 2 tests continue, but must now also be seen as highly speculative; one combines feladilimab with Astrazeneca's tremelimumab and the other includes Bristol Myers Squibb's Yervoy. The CTLA-4 combo strategy was seriously undermined with last year's failure of the Emerge study of Jounce's competing Icos MAb vopratelimab plus Yervoy (Jounce trounced after Icos stumble, November 3, 2020). If the latest setbacks signal the end of feladilimab – the industry's most advanced Icos MAb – this will add to Glaxo's struggles in oncology. The group's anti-BCMA ADC Blenrep did make it across the line in multiple myeloma, but toxicity looks set to limit its use to late-line settings; the anti-PD-(L)1 MAb dostarlimab is still not approved in the US, after a 2020 Pdufa date came and went; and another once-promising late-stage asset, bintrafusp alfa, has failed two important studies.

What next for Icos?			
Project	Company	Mechanism	Status
Oncology			
Feladilimab (GSK3359609)	Glaxosmithkline	Icos agonist MAb	Ph3 <u>Induce-3</u> & <u>Induce-4</u> (Keytruda combos) discontinued; ph2 anti-CTLA-4 combos ongoing
Vopratelimab (JTX-2011)	Jounce Therapeutics	Icos agonist MAb	Ph2 Emerge (Yervoy combo) failed; ph2 Select (JTX-4014 combo) ongoing
BMS-986226	Bristol-Myers Squibb	Icos agonist MAb	Phase 1/2 (Opdivo/Yervoy combo) ends Oct 2022
XmAb23104	Xencor	Icos co-stimulator x anti-PD-1 bispecific MAb	Ph1 <u>Duet-3</u> (Yervoy combo) ends Sep 2024
Autoimmune disease			
ALPN-101	Alpine Immune Sciences/Abbvie	Icos/CD28 antagonist	Ph1 <u>GvHD study</u> terminated; <u>ph2 in lupus</u> starts Jul 2021
MEDI-570	Astrazeneca	Anti-Icos MAb	Discontinued in ph1 (lupus)
Source: company information & clinicaltrials.gov.			

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