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Dermira in a spot of bother after acne failure

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Dermira's DRM01 was supposed to transform the acne arena, but instead the compound is heading for the scrapheap after a spectacular phase III failure. The company will now turn its attention to the excessive sweating candidate DRM04, which is due an FDA approval decision in June.

Dermira also has lebrikizumab, licensed in from Roche, in phase II in atopic dermatitis; topline data are expected in the first half of 2019 (see table below). But the importance of DRM01, also known as olumacostat glasaretil, to Dermira was made obvious today, with the group's stock plunging 63% this morning.

Dermira's pipeline

Project	Indication	Status	2022e sales ($m)
DRM01/olumacostat glasaretil	Acne	Failed phase III	181
DRM04/glycopyrronium tosylate	Hyperhidrosis (excessive sweating)	Filed – PDUFA Jun 30, 2018	154
Lebrikizumab	Atopic dermatitis	Top-line phIIb data due H1 2019	20

Source: EvaluatePharma.

During a conference call today, Dermira's chief financial officer, Andrew Guggenhime, was at pains to point out that the company had $550m in the bank, enough to fund it to its next inflection points. Dermira is now trading below these cash levels, and Evercore ISI's Umer Raffat noted that investor feedback on DRM04 and lebrikizumab in dermatitis had been "lukewarm".

No bright spot

The big hope had been DRM01 – it had been expected to become the third-biggest acne drug by 2022, according to *EvaluatePharma* sellside consensus. Now its future looks dim after two phase III trials, Clareos-1 and Clareos-2, failed to show a benefit on any of the co-primary endpoints studied.

This was a surprise to analysts and investors alike after positive phase IIb data; last month Leerink gave DRM01 a 90% probability of success (*Dermira's acne drug hits the spot in phase II, May 11, 2016*).

In hindsight the fact that Dermira used a completely new dose in phase III might have been a red flag. In phase IIb, both a 4% and 7.5% formulation met the primary endpoints, but the company pressed on with an untested 5% dose, saying today that this was the highest concentration it believed it could produce with sufficient stability for commercial use.

On the conference call Dermira's chief executive, Tom Wiggans, said it was possible that a concentration higher than 5% might have been needed for the project to succeed, but added that this seemed unlikely based on the phase IIb results.

He added that there was no evidence that differences between the phase II and III studies, for example in patient age, had driven the latest failures.

High variability in phase III could have been a factor, and Mr Wiggans said the standard deviation was greater in phase III than in phase IIb – "the opposite of what you'd expect as trial size increases". Meanwhile, Evercore's Mr Raffat suggested that a high placebo response might have done for DRM01.

Whatever the reason, Mr Wiggans admitted that it was "difficult to see a path forward" for DRM01. However, he did not close the door on the project completely, saying: "Should we identify a breakthrough we would of

course evaluate further."

Realistically, though, Dermira's hopes now rest on DRM04 and, later, lebrikizumab in atopic dermatitis – the company picked up rights in certain indications from Roche last year (*Dermira grabs big pharma castoff, August 9, 2017*).

As for whether Dermira would need to bring in any more assets, Mr Wiggans said this might make sense but was not urgent, and the focus for now was on launching DRM04.

Dermira will give more details on its launch plans for DRM04 during an analyst day in May, as well as information on other pipeline projects.

Acne does not seem likely to feature. "It's pretty hard for me to get psyched up about jumping into an acne programme," Mr Wiggans concluded. After the latest stumble – as well as failures from Foamix and Novan last year, which are continuing with their projects – the disorder is looking like an increasingly tough nut to crack.

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