December 2013 in New Orleans suggested that lower doses would reduce the risk of vaso-occlusive events, yet maintain efficacy in most patients. It also highlighted age and prior disease as influencing the rate of cardiovascular events—factors that may find themselves on revised clinical guidelines for the drug's use.

Ariad's drive to return Iclusig to as wide a portion of suitable US patients as possible is understandable: as the company's only marketed drug, it was propping up almost the entire valuation. The company slashed 40% of its workforce and pledged to reduce spending in 2014 by 35%. With cash supplies extended until mid-2015, Berger is confident the firm won't need to go back to investors before Iclusig returns. But to protect itself from an unwanted takeover, Ariad announced a shareholder rights plan—also known as a poison pill—the day after the withdrawal.

Citi Research analyst Jonathan Eckard in New York agreed back then that there would be a path back to market for Iclusig, even when sales might be limited. Eckard believes Ariad remains a "viable company that could turn profitable," thanks also to phase 1/2 non-small cell lung cancer candidate AP26113. Indeed, "our basic strategy is unchanged. We're moving forward with filing [Iclusig] in Japan; [the plan in] Europe is in place, and we will solve these problems in the US," declares Berger, reflecting back on a similar FDA setback experience while head of R&D at Philadelphia-based Centocor (now part of Johnson & Johnson) over 20 years ago.

Berger underlines two lessons from the recent experience. First, be aware that a safety-focused FDA could take a new line on how it accounts for adverse events. Second, consider studying multiple doses in pivotal trials, rather than focusing early on one optimal dose.

Iclusig's withdrawal and re-instatement won't likely affect FDA's accelerated approval pathway or its breakthrough therapy designation, says Citi's Eckard. There will be more Iclusig-like stories, where a first-round approval has to be adjusted. Each time this occurs, "both the Agency and the company will learn from it, and how to optimally approach it," notes Eckard.

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Around the world in a month