Evaluate Vantage

December 09, 2019

# Ash 2019 – Merck gets Arqule ahead of data

Elizabeth Cairns


**Arqule's investors have done pretty nicely out of today's buyout by Merck & Co, but might be wondering whether they could have done better still.**

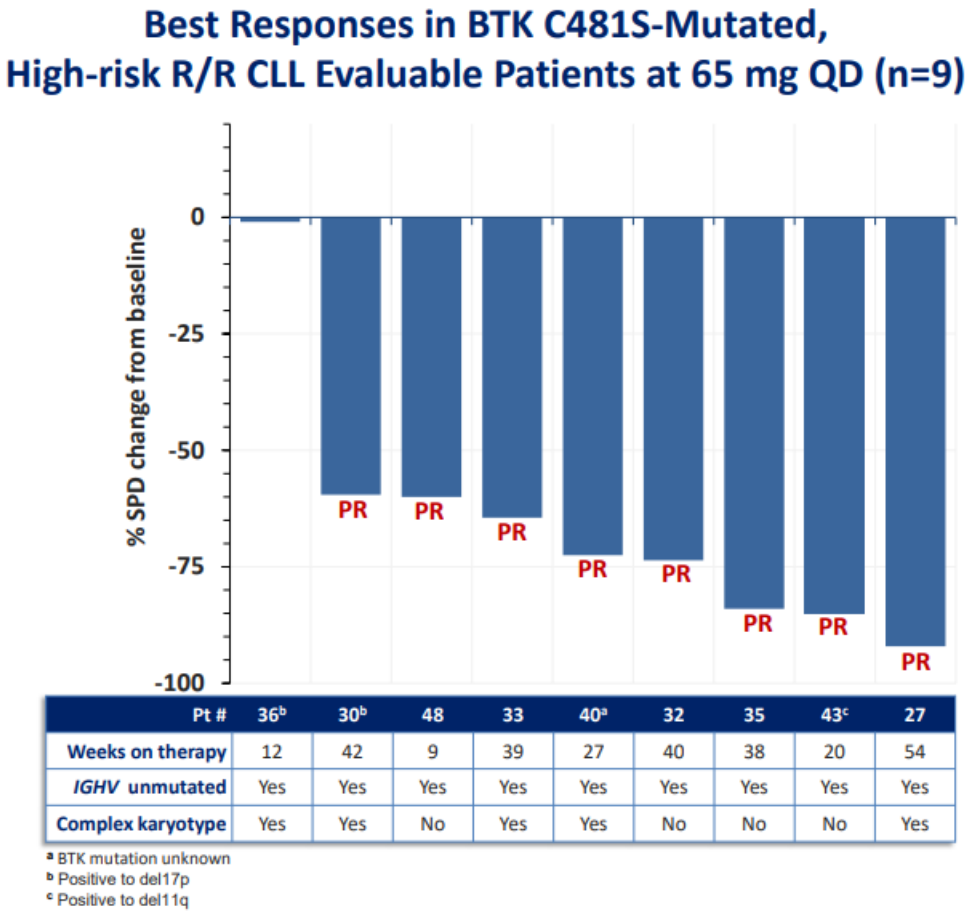
Today's highly encouraging Ash data on Arqule's BTK inhibitor ARQ 531 must have been seen by Merck & Co as the group was putting together its $2.7bn takeover bid. The strength of the data even has some wondering whether Arqule could have extracted an even higher price had it held out before leaping into Merck's embrace.

But those dreaming of bigger premiums should remember that the BTK inhibitor space is incredibly competitive, and the Arqule data still early. And while big pharma does not always get the price of an asset right the market can also get it very wrong. Arqule shares have not been anywhere near the $20 that Merck is offering for almost 20 years, and longer-term shareholders will no doubt be delighted.

**BTK FTW**

The data attracting all the attention at Ash today concern 47 patients with various B-cell lymphomas in a phase I dose-escalation study, which is still ongoing. Patients were heavily pretreated; most had failed on chemotherapy, an anti-CD20/19 antibody and either Imbruvica or Calquence.

Despite this response rates were promising: an overall response rate of 89% (eight of nine) was achieved in chronic lymphocytic leukaemia patients with a BTK-C481S mutation, which is thought to be responsible for driving resistance to existing BTK inhibitors. Activity in these mutants is crucial for ARQ 531 to have legs, so this represents a major validation.



ARQ 531 response rates in CLL, via Arqule's Ash presentation.

ARQ 531 is a non-covalent and reversible BTK inhibitor, unlike J&J's Imbruvica and Astrazeneca's Calquence, and it this thought that this differentiation helps it to work when the others fail. C481S usually develops as a resistance mutation after treatment with a first-generation BTK like Imbruvica or Calquence, so the results in these patients are more or less a home run.

But results were impressive elsewhere too: an ORR of 50% was achieved in six subjects with Richter's transformation, a very aggressive type of lymphoma. Two additional partial responses were generated, one in follicular lymphoma and one in diffuse large B-cell lymphoma.

**Competition**

When earlier data from the same trial were presented at the European Hematology Association meeting this summer it was suggested that reversible BTK inhibitors such as '531 might one day be used before permanent blockers such as Imbruvica and Calquence (*EHA 2019 – turnaround puts Arqule in the takeover frame, June 14, 2019*).

This is starting to look like a real possibility, though even with the might of Merck behind it '531 has a long way to go. Imbruvica is forecast to have sales of $10.3bn in 2024, according to *EvaluatePharma*.

What is clear is that ARQ 531 is the leading reversible BTK inhibitor, though Lilly's Loxo-305 is not far behind. A presentation at Ash detailed an ORR of 77% (10 of 13) in CLL patients treated with Loxo-305, with an ORR of 50% in C481S-mutants. The latest data on Sunesis Pharmaceuticals' rival asset vecabrutinib show that three of five patients treated with 300mg achieved stable disease, but no remissions have been reported.

Durability remains a key test of these agents, but for now the signs are promising. And with another non-covalent BTK inhibitor in the hands of big pharma, these projects will be pushed forward quickly.

+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754