

## Five Prime looks to turn a corner



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### Survival data with bemarituzumab see the company erase half of the past three years' losses.

With Five Prime's stock surging 300% overnight the company will be hoping to put a disastrous three years behind it. The reason for the sudden enthusiasm lies in survival data with bemarituzumab, a wholly owned asset the group had touted last year, but which until now had little to back up the hype.

The findings, in the Fight trial in first-line stomach cancer, position the company's lead project as the first mover in a new approach, FGFR2B inhibition, with little competition. Of course they come with caveats, and the stock move has to be seen in the context of a share price that had lost 90% of its value since 2016.

The collapse in 2016/17 was triggered by disappointing data with cabiralizumab, an anti-CSF-1R MAb partnered with Bristol Myers Squibb. A restructuring and C-suite sweep-out followed ([Five Prime moves towards subprime, January 16, 2019](#)). Five Prime's phoenix-like rise sees it valued at \$800m, which by today's standards seems undemanding.

#### Taking the Fight

The spotlight now falls on bemarituzumab. Fight was the first large trial in front-line gastric/gastroesophageal junction cancer to screen for FGFR2B overexpression, which the company says accounts for 30% of non-Her2-driven cancers of this type; according to last year's investor pitch this amounts to 56,870 addressable patients.

[Fight combined bemarituzumab with chemo](#), and compared its progression-free survival versus chemo alone as primary endpoint; overall survival was a secondary measure. Both showed a statistically significant effect, according to the study's design, with median PFS improving 2.1 months to 9.5 months, and median OS not yet reached but showing a 42% reduction in risk of death.

This is where the caveats begin, however. Five Prime revealed that the p value threshold for this trial was 0.2, and according to this both measures succeeded, with  $p=0.073$  and  $0.027$  respectively. Had Fight used the more common definition of statistical significance of 0.05 the study would have been a bust, since its primary endpoint would have missed this stricter threshold.

The group defended its design, saying this was not uncommon for a small phase II study; it said it had not designed Fight as a registrational study, and had only been hoping to see a survival trend. As such, the seemingly positive data appear to have come as a big surprise.

#### Questions

If Five Prime now seeks to raise cash, potential investors will question why the upper bound of the confidence interval for PFS is above 1.0, and why 34% of bemarituzumab subjects discontinued because of an adverse event versus just 5% in the control group. And nothing has been said about baseline patient characteristics, an imbalance in which could account for the apparent benefit.

A further spanner in the works is that the front-line setting is set to change, with Merck & Co and Bristol both recently claiming successes with anti-PD-1 antibodies, though histology and biomarkers complicated data interpretation (*Esmo 2020 - double win complicates the gastric cancer picture*, September 21, 2020).

If FGFR2B is indeed implicated in gastric cancer competing companies should take note. *EvaluatePharma* data reveal several with assets against this target, though apparently none with specificity at the 2B subtype. While bemarituzumab is an antibody most are small molecules; Incyte's Pemazyre, which hits FGFR1/2/3, is marketed for cholangiocarcinoma.

Five Prime also claims that FGFR2B is overexpressed in subgroups of squamous NSCLC, triple-negative breast, ovarian and pancreatic cancers. For now, however, its focus must be on designing a phase III gastric cancer study with a primary endpoint of OS.

Selected clinical assets with activity at FGFR2			
Project	Company	Target	Type
<i>Marketed</i>			
Pemazyre	Incyte	FGFR1, 2 & 3	Small molecule
<i>Phase II</i>			
E7090	Eisai	FGFR1, 2 & 3	Small molecule
Debio 1347	Debiopharm/Roche	FGFR1, 2 & 3	Small molecule
HMPL-453	Hutchison China Meditech	FGFR1, 2 & 3	Small molecule
ABSK091	Abbisko Therapeutics	FGFR1, 2 & 3	Small molecule
Bemarituzumab	Five Prime/Zai Lab	FGFR2B	Antibody
<i>Phase I</i>			
3D-185	3D Medicines	FGFR1, 2 & 3, CSF1R	Small molecule
DS-1123	Daiichi Sankyo	FGFR2	Antibody
RLY-4008	Relay Therapeutics	FGFR2	Small molecule
PRN1371	Sanofi (ex Principia)	FGFR1, 2, 3 & 4	Small molecule
<i>Source: EvaluatePharma &amp; company statements.</i>			

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