

## Bionomics fail leaves Oxigene as last one standing



Jacob Plieth

If it is curious that this morning's failure of Bionomics' lead project, BNC105, in renal cancer did not cause the Australian group's stock to fall more than it did, the dip in Oxigene shares can also be questioned.

After all, the phase II flop effectively leaves Oxigene as the last company with a vascular disrupting agent in mid-stage clinical development. In Bionomics' case, perhaps a data-mining operation, picking out numerous biomarkers that it said were associated with disease control for the first time, averted a bigger share price blowup.

Vascular disrupting agents were once hailed as a highly promising oncology strategy, but numerous setbacks whittled the field down to two players: Bionomics and Oxigene. The latter celebrated an unexpected win just last week with Zybrestat in ovarian cancer, prompting its stock to double ([Oxigene soars on surprisingly positive news from disappointing drug class](#), March 12, 2014).

No such luck for Bionomics, which today revealed that in the Disruptor-1 trial in 139 renal cancer patients who had already failed on two tyrosine kinase inhibitors, BNC105 combined with Novartis's Afinitor had failed to prolong disease-free survival versus Afinitor alone.

Bionomics closed down 30% on the Australian stock exchange today, while Oxigene's Nasdaq-listed stock was off 3% in early trade. The US biotech is still valued at only \$45m, and important data from its Zybrestat trial, like the actual numerical PFS benefit in each arm, have yet to be revealed; perhaps the Bionomics failure has been seen as a sign that the full Zybrestat results are unlikely to overwhelm.

### Subgroup analyses

The Australian group has opted for touting positive subgroup analyses. In 26 patients with liver metastases, for instance, it said the addition of BNC105 to Afinitor increased PFS from 2.8 to 6.6 months, though the sample was too small to make this significant.

There were also positive trends in patients who had a kidney removed, it claimed, and identified seven biomarkers whose presence correlated with clinical benefit from treatment with BNC105 plus Afinitor. These include macrophage inflammatory protein-1 beta, IL1-beta and alpha-2 macroglobulin.

The plasma biomarkers had previously been associated with BNC105 activity, and thus their analysis formed part of a prespecified exploratory endpoint. Statistically significant disease progression improvements in patients with these biomarkers were hit at six months with p values of 0.0136 to 0.0348, Bionomics said.

BNC105 is also in a phase I/II study in partially platinum-sensitive ovarian cancer due to end in October, and Bionomics also has a small pipeline that includes an anxiolytic partnered with Ironwood Pharmaceuticals. But the group's cash reach is not great; it had A\$20.5m (\$18.7m) at the end of calendar 2013, and this is unlikely to last much more than another 12 months.

Far from bemoaning a failed trial, however, Bionomics said the data dredge was compelling, marked significant progress in validating BNC105 as an anticancer, and showed the best way forward to maximising the project's utility. Remarkably, it hopes that the study will lead to a deal, and that further trials will thus be funded by a partner.

Realistically, however, it needs to run a robust, prospective trial, and not the sort of questionable adaptive-design study that it is now proposing. Investors must surely realise that this will have to be paid for by Bionomics; in other words, they had better brace for a fund raising.

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