EP Vantage interview - Radio-diagnostic specialist seeks new therapeutic frontier

Radiation therapy has been a part of cancer treatment for longer than chemotherapy and, while advances have been made, more effective delivery techniques have been few and far between. Spectrum Pharmaceuticals’ Zevalin is now marketed in non-Hodgkin lymphoma, but has disappointed commercially, whilst high hopes are being placed on Algeta’s phase III Alpharadin in metastatic prostate cancer, to name two drugs that have combined chemical delivery with radioactive compounds.

However, it is an untapped market that big pharma should show greater interest in as it combines therapeutic and diagnostic aspects in a single product, making both efficacy and safety easier to demonstrate, Stefano Buono, chief executive of Advanced Accelerator Applications (AAA), tells EP Vantage. “It’s an unexploited niche that has huge potential,” says Mr Buono, whose company is preparing phase III trials of neuroendocrine tumour (NET) candidate lutate, which the company is calling Lutathera.

“But it’s much simpler to develop a drug in nuclear medicine because you can image. You can quantify in every organ how much is reaching it. You can calculate if it sufficient to affect the target,” as well as easily see off-target effects.

“The first dose can be a diagnostic dose,” he says. “If the receptors are not engaged and it goes into the liver, you don’t use it.”

Spin off

A spinoff of CERN, the European Organisation for Nuclear Research, AAA was formed in 2002 to commercialise discoveries for use in molecular imaging. Its chief asset is fluorodeoxyglucose (FDG) a radiotracer used in positron emission tomography (PET). FDG is used in Gluscan and Gluscan 500, both used to assess glucose metabolism for diagnosing central nervous system and cardiovascular disorders, cancer, and infectious, autoimmune and inflammatory diseases.

FDG does not have strong intellectual property protection, Mr Buono says, a vulnerability counterbalanced by complexity and short shelf life that AAA has responded to with its manufacturing and distribution network. More recently, the company in-licensed imaging products from the Austrian biotech Iason and Italian firm Bracco, as well as acquiring Gipharma for its single photon emission technology agent.

Interest in radiopharmaceuticals is a more recent development. A major partnership with academic institutions formed in 2009 launched preclinical research into theranean, a brachytherapeutic treatment in solid tumours. More recently, with the acquisition of Missouri-based BioSynthema in 2010 it brought in Lutathera, an orphan treatment that it is targeting for mid-gut NETs in a phase III trial against Novartis’ Sandostatin LAR. Compassionate use programmes are being applied for in several European countries.

Lutathera targets somatostatin receptors over expressed on NET cells and, once bound, delivers a radiotherapeutic payload. In phase II trials it demonstrated progression free survival of 44 months.

A third product, even more recently acquired from Dompe in August 2011, is FabOvar, an antibody delivering iodine-131 to ovarian carcinoma.

R&D funding

Mr Buono believes AAA is better positioned than traditional biotechs to develop such drugs and bring them to key development milestones. With an established business generating cash, it does not face the perennial fundraising issues of small biotechs. The privately held firm – a majority of its 88 shareholders are individuals as of the end of 2010 – generated sales of €27.4m ($36.2m) and net profit of €1.7m in 2010, the last full year for which figures are available, and had $11m cash at that time.
“We are profitable because we have a successful business, and we can do that because we have a small niche,” Mr Buono says. “This means we can support our R&D even as we enter costly clinical studies.”

However, that is not the scale of company that could likely launch a drug on its own, much less take on the likes of Novartis and Pfizer, whose Afinitor and Sutent are marketed in NETs. And with the obvious exceptions of Zevalin and Alpharadin, radioactive imaging and radiotherapies are not something big pharma has necessarily pursued with vigour.

The value is that a small initial dose can be used to discover, for example, whether a patient's somatostatin receptors are over expressed on NET cells, and whether Lutathera is a suitable treatment. AAA argues that this is personalised medicine made simple, overcoming the regulatory and commercial challenges of developing companion diagnostics.

“This is why we think this has a lot of unexploited potential,” says Mr Buono. “We have to make big pharma know it is something they can handle.”

Which is perhaps the biggest challenge AAA faces.