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Driving a step change in the treatment of cancer

There are over a hundred different types of blood cancer with the forms of leukemia, lymphoma and myeloma being the most common. Every 3 minutes someone in the US is diagnosed with a blood cancer.

For solid tumours, the most common cancers include breast, lung, colon and prostate.

Andrew Parker, CEO of Step Pharma, discusses his motivation to lead the Company to focus on a novel target, CTPS1, which is considered to be an Achilles Heel of cancer, in the search for highly selective, safe and effective treatments for both blood cancers and solid tumours.

What was your motivation to join Step Pharma?

I have always been intrigued by how a single mutation in our DNA can be irreversibly disruptive, leading to the transition of a normal cell into a cancerous cell. The human genetic story of how a mutation resulting in the loss of CTPS1, a key enzyme that is required for the synthesis of DNA and RNA, leads to the understanding that this could be a novel approach to treat lymphoma exemplifies this concept.

Humans with CTPS1 deficiency demonstrated an impaired capacity to proliferate lymphocytes but importantly have no other negative consequences. This highlighted that inhibiting CTPS1 could be a targeted approach to treat lymphoproliferative disorders such as leukemia and lymphoma without the side effects often seen with cancer drugs. This level of genetic validation is very compelling and quite unusual in drug discovery. The Company's deep understanding of CTPS1 biology and chemistry has ultimately led to the discovery of STP938, a selective CTPS1 inhibitor with excellent pharmaceutical properties.

Consequently, I was convinced by the scientific concept, coupled with the belief and passion of the founding scientists and the enthusiasm of the investors.

In joining Step Pharma in 2019, I had the opportunity to lead and build a team of like-minded drug developers who are focussed on bringing about highly selective cancers treatments without the significant side effects associated with current and emerging cancer therapies.

You've previously worked in senior roles in pharma across other disease areas. How are you applying this experience as CEO of a cancer biotechnology company?

I have had many different roles across big pharma, biotech and VC, each of which has always taught me something new. Drug development requires deep knowledge of the disease area so it is essential to have the right minds engaged. The team at Step Pharma is a perfect balance of deep understanding of oncology, in particular blood cancers, as well as the organisational and drug development skills required to successfully advance a small molecule program.

The biotech CEO role is focused on the bigger picture, building the right team, setting the strategic direction, ensuring we have enough money to succeed, but the most important thing I have learned is to never allow this to disconnect you from the science and the detail of the preclinical and clinical data.

What is the issue you are trying to solve with current treatments for T cell and B cell malignancies?

The successful treatment of lymphoma, which develops from white blood cells called lymphocytes, is quite different when comparing T cell with B cell lymphoma. In all cases the frontline therapy is chemotherapy which brings a successful outcome for many patients but is associated with significant side effects. However, a significant number of patients treated with chemotherapy will relapse.

For B cell lymphomas there are a range of second-line and third-line drugs which offer limited benefit for these patients and a significant number will still relapse. In T cell lymphomas there are very few second line agents and none of them are particularly effective.

We aim to bring forward treatments that will add to the armoury of options for B cell lymphoma patients and transform the way T cell lymphoma is treated.

Why is CTPS1 inhibition going to address this need?

Targeting the pathways that make nucleotides, which are required for the synthesis of DNA and RNA, is a well explored and validated concept in oncology. However, until now this has been achieved through non-selective drugs, which cause unacceptable side effects.

Human genetics and the identification of a handful of individuals that lack CTPS1 demonstrated the crucial role that CTPS1 plays in allowing lymphocytes, T and B cells, to proliferate. Importantly, the lack of CTPS1 in these individuals had no other effects. This means that selective inhibition of CTPS1 should block proliferation of cancerous T and B cells and not bring unexpected side effects. The reason this can be achieved is due to the related enzyme CTPS2 which is able to maintain nucleotide synthesis in healthy cells, something unique to this step in the pathway and a key differentiation for our approach.

Targeted therapies for cancer is a crowded and challenging space, what makes Step Pharma stand out from others in the field and why do you believe you will succeed?

We believe that our investigational therapy, STP938, has the potential to transform the way lymphomas are treated. T cell lymphoma patients have no good options following relapse and there are few alternative drugs in development. The high unmet need for novel therapies brings the potential for the accelerated approval of STP938 following successful Phase II clinical studies.

B cell lymphoma treatment is complex and, despite the recent success seen with CAR-T therapies, many patients are not fit enough to withstand the trauma of a CAR-T therapy. As more data accumulates, it is becoming clear that the majority of CAR-T patients will also relapse. The future of cancer treatment lies in moving away from chemotherapy and towards the use of appropriate combinations of targeted therapies to maximise the benefit to patients. These combinations should be driven by science, and we have spent considerable time developing an understanding of the most appropriate drugs that could ultimately combine with STP938.

We also believe that inhibition of CTPS1 will be successful in the treatment of some solid tumours. We are developing a biomarker that will enable selection of patients sensitive to CTPS1 inhibition, with an initial focus on ovarian and lung cancer, aiming to start clinical studies next year. In addition, the combination of STP938 with drugs that inhibit the DNA Damage Response pathway has shown incredible synergy in pre-clinical experiments across a range of solid tumours.