Frequently Asked Questions

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Science / Pipeline

VAL201

What phase of development is VAL201 at?

VAL201 completed a Phase 1/2 clinical trial in the treatment of patients with prostate cancer in 2020. The results from this trial underwent an initial analysis, and readout that the treatment was seen to be safe and well tolerated at the dose levels administered, and that 54.5% of patients "responded" to the treatment, that is that their cancer did not progress during their period on trial.

Drugs are typically progressed through Phase 1, Phase 2 and Phase 3 clinical trials, with at least one trial being run at each stage before being considered for authorisation for use in the general patient population.

What can we expect to happen next for VAL201?

ValiRx is currently in the process of identifying a partner to progress further scientific development of VAL201. Such a partner would be able to fund a larger trial to look in greater detail at the activity of VAL201 in patients, with the confidence of knowing they are building on the encouraging results we have already gathered.

The exact nature of the partnership and of the next clinical trial will depend on the identity of that partner, but the next stage of scientific development is expected to be a full Phase 2 clinical trial.

Are the clinical results sufficient for progress?

The results from the Phase 1/2 clinical trial of VAL201 can be considered from two angles. Firstly, the safety and tolerability of the treatment was seen to be excellent. As this was a first-in-man trial, safety is always the first consideration, to ensure that the principle of "first do no harm" is fulfilled.

Secondly, the assessment of whether the treatment provides a positive disease impact returned the result that 54.5% of patients responded to treatment by not seeing any disease progression during the trial. Although this only considered 11 patients (with 6 responding) across multiple dose levels, this early indication of disease impact supports the conclusion that further research is warranted.

Why were so many side effects reported as being due to administration of VAL201?

In our announcement of 28 September 2020, we listed all of the events that were recorded as being related to the administration of VAL201. The minor events reported were either temporary, so subsided within a matter of hours, or were judged not to cause a disproportionate hindrance to the daily life of the patients. Minor events of this type are typical in cancer drug trials.

The 'injection site disorders' covers events ranging from discomfort at the site of the injection, a slight temporary rash at the site of injection, or a bruise. These would be common during any injection process.

The other minor effects reported included raised blood pressure, bradycardia (low heart rate), fatigue, dyspepsia (indigestion) and muscle spasm. All of which are typical minor side effects from cancer drugs.

The only “serious” drug-related event was the severe raised blood pressure (hypertension) in one patient at 8 mg/kg. This patient had a history of hypertension and, after treatment with an anti-hypertensive drug, continued in the trial at the same dose.

It is important to see these adverse events in the context of the disease and current drugs. The treatment of prostate cancer by existing hormone deprivation therapy has debilitating side effects related to reduced testosterone levels. None of these side effects were reported for VAL201, adding to the evidence that VAL201 acts with a very precise mechanism, preventing testosterone driven cancerous growth and avoiding related side effects that reduce patients’ quality of life. Furthermore, the more severe effects typical of traditional chemotherapy were also not seen, such as nausea, weight loss, hair loss and extreme tiredness.

All drug related events recorded by our patients are important and must be assessed further in future clinical trials. Nevertheless, the safety and tolerability of VAL201 as demonstrated in this trial is excellent.

VAL301

What phase of development is VAL301 at?

VAL301 uses the same active ingredient as VAL201, but proposes the treatment of women with endometriosis. VAL301 is in preclinical development. As it uses the same ingredient as VAL201, the safety and tolerability data collected during the clinical trial, and preclinical safety data collected to support that trial can also be used to support development of VAL301. However, additional preclinical work is required to ensure that the treatment does not adversely affect otherwise healthy women, as the prostate cancer trial only enrolled men with a terminal cancer diagnosis.

What can we expect to happen next for VAL301?

A clinical development plan has been compiled that considers several different clinical trial designs and the level of preclinical safety data that would be needed to collect to enable them.

What is the Japanese Pharma partner evaluating, how long will it take, what is likely to happen when they finish?

On 1st May 2020 we announced that ValiRx had entered into an agreement with an undisclosed Japanese Pharma company to enable the Japanese company to evaluate VAL301 in their own lab for use in an endometriosis development programme. This agreement detailed a number of preclinical experiments to explore specific scientific details of interest to that company, including compatibility with a proprietary delivery system.

As these experiments are being carried out by a third party, ValiRx has neither control nor knowledge of progress of these experiments. We remain in close contact with the Japanese company, and discuss other aspects of the program (such as the impact of the VAL201 safety data on the VAL301 program). When they conclude their evaluation, and if results show alignment with their strategy, we expect to enter a period of negotiation during which we will determine if there is a mutually acceptable route for development of the project.

The outcome of the negotiation could result in a number of commercial arrangements, such as a joint venture, a collaborative research programme, or a regional or global licensing arrangement.

In the meantime, ValiRx is actively presenting the project to other partners with a view to developing options for developing the programme further in collaboration with other appropriate partners, whether or not the Japanese company wishes to participate in any such arrangement.

VAL401

What phase of development is VAL401 at?

VAL401 completed a pilot Phase 2 clinical trial in end-stage non-small cell lung cancer patients. This trial demonstrated an improvement in patient survival when compared to case matched patients in the same clinics who were not enrolled on the trial. The patients also reported improvements in quality of life, including improvements in pain, nausea and appetite.

On analysis of the results of this trial, independent oncologists recommended the next trial to be in patients with pancreatic ductal adenocarcinoma (pancreatic cancer) who typically present with symptoms with particular burdens of pain, nausea and anorexia.

What can we expect to happen next for VAL401?

A clinical trial has been planned to treat newly diagnosed patients with standard of care in conjunction with VAL401, in a blinded comparison against standard of care with placebo in around 120 patients.

This clinical trial is outside the remit for direct ValiRx invovlement, and external partners are being sought to further this development.

Is the agreement with Black Cat Bio still in place?

On the 14th January 2020, ValiRx announced that the subsidiary, ValiSeek, which olds the VAL401 asset had entered into an agreement with an independent company, Black Cat Bio Limited, in order to seek external funding and partners for the VAL401 project. This agreement is still in place, and Black Cat Bio provides regular updates on progress on their efforts to secure funding to advance the programme.

The agreement is only relevant to VAL401, and not any of the other ValiRx programmes.

KTH222

What stage of development is KTH222 at?

KTH222 is currently in preclinical development for the development of ovarian cancer.

What can we expect to happen next for KTH222?

KTH222 is currently subject to an evaluation agreement from Kalos Therapeutics to ValiRx. If the experimental programme is successful, ValiRx will look to enter a full license agreement with Kalos. As announced on 10th November 2020, this is likely to be in the format of a Joint Venture agreement whereby a new subsidiary of ValiRx is set up to hold the project, and is jointly owned by both ValiRx and Kalos. This JV will then be funded by ValiRx to continue the preclinical development steps while seeking external funding and partners to take the programme into clinical trials.

BC201

How does BC201 work?

BC201 incorporates the VAL201 peptide as a component of a possible treatment for patients suffering severe symptoms of Covid-19. The mechanism of action for VAL201 in this application should be considered from several angles.

- Firstly, the link between the levels of expression of the Androgen Receptor on cells and susceptibility to severe symptoms of Covid-19 are clear and well published. Treatment with VAL201 has the potential to moderate activity of the Androgen Receptors and expression of the protease TMPRSS2, which is required alongside the ACE2 receptor for the virus to enter the cell, thus reducing infectivity.
- Secondly, the role of VAL201 in blocking the hormone mediated activity of SRC kinase is proposed to have a direct impact of the production of Neutrophil Extracellular Traps (NETs). These NETs are part of the immune response and are initially helpful for removing virus (or bacteria) after an infection. In severe cases of Covid-19, just as in sepsis, these NETs can cause bystander collateral damage, causing multi-organ failure, which triggers further production of NETs and perpetuates the cycle. By breaking this NET cycle, severe symptoms caused by the over-reaction of the immune system is moderated. It is not as straightforward as an "anti-inflammatory effect".
- Finally, as the virus uses the infected cell's internal machinery to replicate, the inhibition of a key pathway by the VAL201 peptide, may also slow the replication rate of the virus, giving additional time for the immune system to respond appropriately.

This multi-faceted approach is considered a key advantage of the BC201 programme, and the consortium developing BC201 is investigating each benefit individually, as well as in synergy.

Can BC201 be fast-tracked to patients?

The processes for fast-tracking medicines to market approval and patient access are driven predominantly by the level of medical need of those patients. For example, patients suffering a disease for which there are few marketed treatments available may be able to access treatments that are still in development.

The Coronavirus pandemic has provided an extreme example of both treatments and vaccines being fast-tracked to receive emergency use authorisation in patients.

BC201 combines VAL201, which has achieved an excellent safety and tolerability profile in the Phase 1/2 clinical trial, with other agents that are recognised as "safe". This profile allows us to propose this for emergency use while preclinical experiments are initiated to further explore the scientific rationale. The broad nature of the mechanism of action for immune modulation allows for further development of the programme into the treatment of sepsis, and to be ready for future pandemics.

What stage of development is BC201 at?

BC201 is undergoing preclinical experiments to assess whether the theoretical mechanism of action is demonstrated in appropriate biological systems. The development is being carried out by the consortium that has been formed between ValiRx, OncoLytika and Black Cat Bio. This consortium has commissioned the experimental work to date, is applying for UK government grants, and actively seeking development partners to progress the project.

What can we expect to happen next for BC201?

BC201 continues to be developed for treatment of patients in the current Coronavirus pandemic, but also with a view to widening usage to viral-induced sepsis and other diseases with similar immune system driven causes.

The next steps will be to complete the preclinical work and to commence regulatory proceedings if a clinical trial is planned outside of the emergency pandemic situation.

Corporate / Financing

What are the financial implications if the Japanese company TAKE ON 301 and possibly 201?

The Japanese Company with whom we have a Material Transfer Agreement (as announced on 1st May 2020) has a particular interest in developing a women's health product, so, while VAL301 fits their strategy well, there is no indication of any interest in VAL201.

If the Japanese Company wishes to develop VAL301 beyond their current evaluation, they will be able to consider a selection of standard options such as global or regional licensing with a mixture of upfront, milestone and royalty payments. In the case of a regional license, ValiRx would retain rights to other regions and be able to co-develop the project, or to license to additional partners.

How will ValiRx generate income or return on investment?

A priority for ValiRx is to secure near-term funding by out-licencing or partnering the existing clinical programmes (VAL201 and VAL401). We are in active discussions with a number of companies to achieve this.

In the longer-term, the strategy we introduced last year sees revenues entering the Company from two sources.

Firstly, our strategy for creating subsidiary companies and assisting in their operation is intended to bring fees into ValiRx, which we expect to cover day-to-day working capital requirements as the business builds. This will be via service contracts between each subsidiary and ValiRx, whereby ValiRx will continue to provide the corporate framework in which the subsidiary can operate, including, for example, project management resource, IT and accountancy functions.

Secondly, we expect to retain an equity interest in each subsidiary, so that ValiRx will benefit from an exit event, e.g., out-licence or sale.

The exact timing of the first revenues to enter the Company is difficult to predict, but we are confident that the strategy is the right one for the Company, and will result in the most efficient route to revenues.

When will the first drug be brought to market?

ValiRx aims to partner projects during the development process, such that drugs within the ValiRx pipeline are unlikely to be brought onto the market directly by ValiRx. As specialists in discovery, preclinical and early clinical phase development, ValiRx adds value at the early stage of drug development. The projects ready for late stage clinical development will be passed to specialists in this stage, and then likely onto commercialisation specialists who will bring the drugs to market.

VAL201 has completed a Phase 1/2 clinical trial, so is required to complete Phase 2 and 3 before market authorisation can be considered – the timeline for this will be dependent on the design of those trials. VAL301 is at preclinical stage, so requires all three clinical phases of development. VAL401 has a shorter route to market due to the nature of it as a reformulated generic drug, and requires at least one further clinical trial (depending on size and results) before market authorisation could be considered.

Therefore, of these three pipeline products, VAL401 can be considered furthest along the development pipeline. However, the timing of market authorisation is difficult to predict, especially as it is controlled by a third party.

Who is going to fund the programmes further?

Our preferred business model is to partner projects at the earliest feasible stage in order to reduce risk, reduce direct cost, and to increase the range of skills and expertise being input to the project. Each project has different needs in a partner and will be assessed accordingly.

VAL301 has an agreement already announced with a Japanese Pharma Company, whereby the third party is covering the costs of the current developments and sharing the information generated.

Partner identities can be released only when agreements have been finalised in order to avoid prejudicing ongoing negotiations. Even when an agreement is reached, there can be continued restrictions on announcing the identity of the partner according to their own corporate policies. However, all partners will be selected for their suitability to continue the science, with resources and expertise as a prerequisite.

COVID-19

With Covid restrictions increasing, will this affect product progress?

As announced on 19 May 2020, the Company identified that there was a possibility of a delay in processing the data from the VAL201 clinical trial due to restricted access to the clinical unit at University College Hospital (UCLH) in London during lockdown. As the database is now locked, this is no longer a factor in our timelines.

With variable pandemic restrictions across the UK, ValiRx is very fortunate to have a flexible team that can work remotely, and productivity is predominantly unaffected by local restrictions. We will assess the Covid risk for all projects and take mitigating actions should they be required.