



Non-confidential VAL201 Prostate Cancer

Q1 2021



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VAL201

Indication:

- Prostate Cancer
- Phase 1/2 clinical trial recently completed in 12 adult men, with incurable locally advanced or metastatic prostate cancer who have relapsed following radiotherapy treatment

Mode of Action:

- Inhibition of the interaction of the Androgen receptor with the SH3 domain of SRC kinase.
- This precision inhibition allows other functions of both androgen and SRC kinase to continue as normal, reduce side effects

Product:

- VAL201 is a decapeptide, presented as a lyophilised powder for once weekly sub-cutaneous injection in PBS

Status:

- Phase 1/2 clinical trial completed. Headline results demonstrated 55% response rate of patients showing no progressive disease via PCWG2 criteria. PSA doubling times were observed to increase after treatment ($p < 0.05$)
- The drug was safe and well tolerated.
- In discussion with potential partners

USP:

- The precision mechanism allows for the treatment of cancer without the normal side effects from androgen deprivation
- The novel mechanism enables treatment of patients for whom resistance to other treatments may already be apparent (for example with castrate resistant tumours)

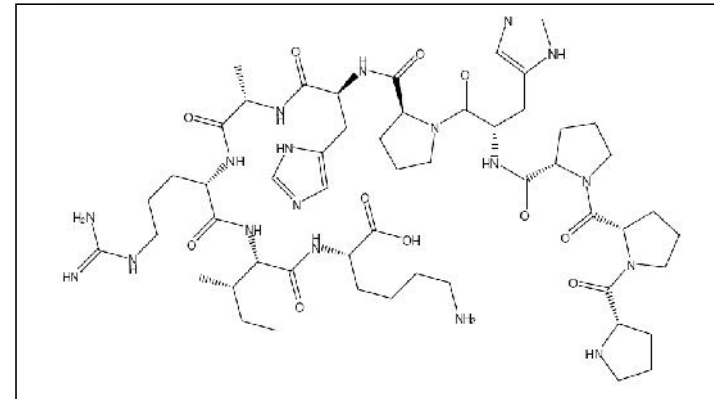
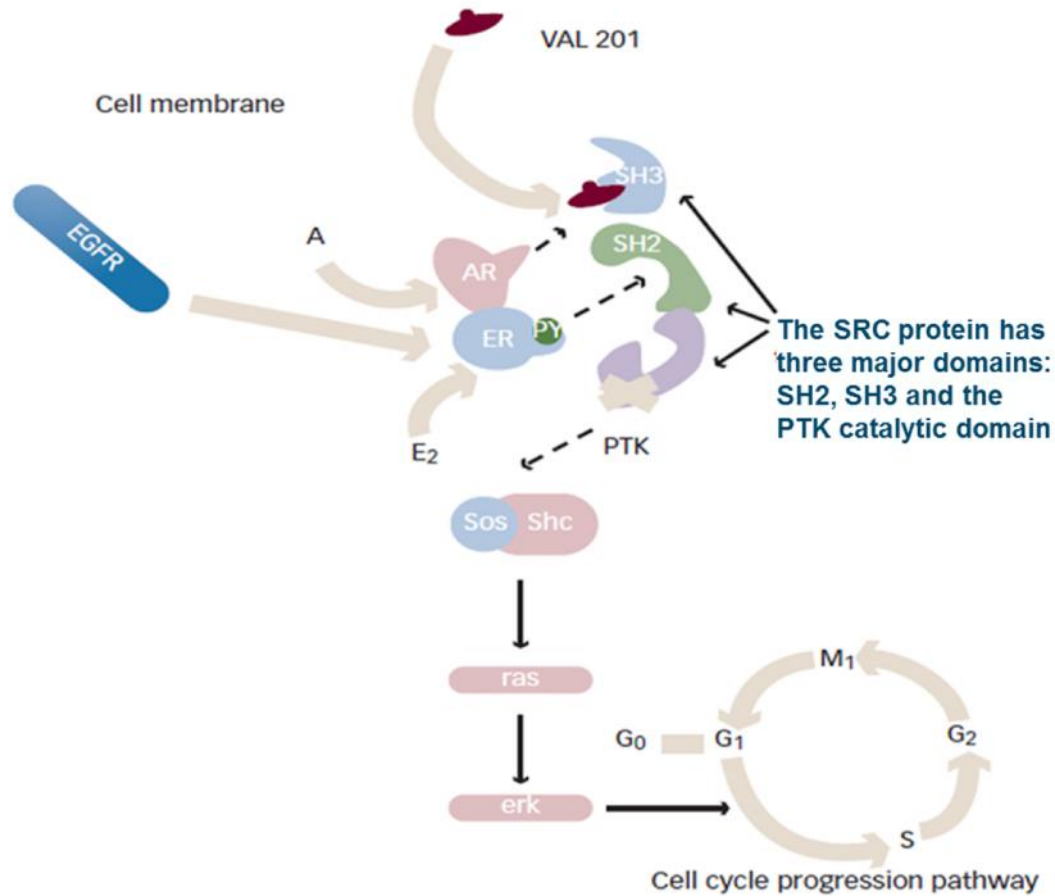
VAL201 summary and timeline



VAL201 is a decapeptide designed for the treatment of patients with prostate cancer. Administered once weekly as a sub-cutaneous injection, early clinical data supports further development of the project

| | |
|----------------------------------|---------------------------------|
| Phase 1/2 Clinical Trial Started | 19 th December 2014 |
| End of Trial | 27 th January 2020 |
| Database lock | 4 th September 2020 |
| Official Headline results | 28 th September 2020 |
| Clinical Study Report available | January 2021 |

VAL201 mechanism

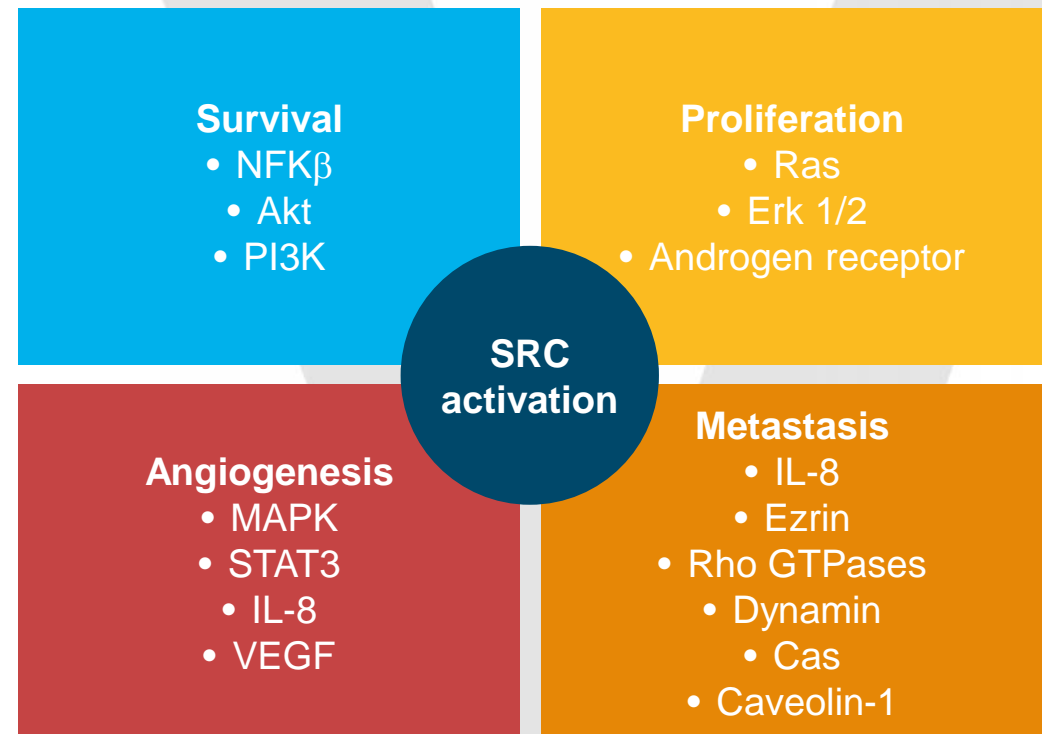


| H-Pro-Pro-Pro-His-Pro-His-Ala-Arg-Ile-Lys-OH | |
|--|---|
| Molecular Weight (free base) | 1149.3481 |
| Molecular Formula | C ₅₅ H ₈₄ N ₁₈ O ₁₁ |
| Melting Point | 186° C |
| Solubility | Freely soluble in water |
| pH of a 1% solution in water | 5.67 |
| Salt Form | acetate |

Rationale for SRC inhibition

- SRC family kinases (SFK) are non-receptor protein tyrosine kinases whose activity is increased in most solid tumours
- In the active state, SRC interacts with downstream substrates to facilitate signal transduction
- SRC activation in prostate cancer:
 - Promotes tumorigenesis
 - Is an important mediator of androgen receptor signalling and cell proliferation
 - Promotes pro-metastatic properties
 - Promotes angiogenesis and vascular permeability
- Inhibitors of SFK universally inhibit prostate cancer cell proliferation in vitro
- SRC inhibition is therefore expected to have beneficial effects in prostate cancer treatment

Activation of SRC family kinases stimulates signalling pathways involved prostate cancer progression



VAL201 Advantages

- Inhibition of SRC kinase interaction with the Androgen receptor:
 - Inhibits androgen-induced proliferative activity of SRC kinase**BUT**
 - Without preventing kinase activity
 - Without impacting other activity of the androgen receptor
- Due to close proximity to Estrogen Receptor binding site, similar activity and side effect profile expected for estrogen-induced proliferation
- Low side effects expected due to target precision

VAL201 Phase 1/2 Clinical Trial Completed



A Phase III, Dose Escalation Study to Assess the Safety and Tolerability of VAL201 in Patients with Locally Advanced or Metastatic Prostate Cancer and Other Advanced Solid Tumours

12 patients dosed between 0.5 mg/kg and 8 mg/kg (prostate cancer only)

Adult men (over the age of 18), with incurable locally advanced or metastatic prostate cancer who have relapsed following radiotherapy treatment, are in 'watchful waiting' or where a policy of intermittent hormone therapy had been decided. Patients expected to have no or only mild symptoms relating to their cancer.

Once weekly dosing by sub-cutaneous injection in PBS

Headline Results confirmed in Full Results released 30 November 2020

- VAL201 is confirmed as a safe and well-tolerated drug candidate worthy of further investigation
- **54.5% Response rate** as assessed by non-progressive disease by PCWG2 criteria
- Statistically significant ($p < 0.05$ by two-tailed Wilcoxon Signed Rank test for paired samples) increase in PSA doubling time post-treatment compared with pre-treatment
- Safe and well tolerated: the only serious treatment-related adverse event was a rise in blood pressure in a patient with pre-existing hypertension

VAL201 Disease Impact Data



- **Disease Impact** measures include PSA values measured at approx. 3 week intervals; and tumour measurements of primary prostate tumour, contributing to **assessment under PCWG2**
- **Headline results** revealed **6 out of 11 patients** showed no disease progression by PCWG2 guidelines during their period on trial
- Full results are available to download from our website at <https://www.valirx.com/our-pipeline/val201> including a breakdown of the disease characteristics of the patients and individual tumour responses
- The Clinical Study Report concludes that the results demonstrate that the project warrants further development

VAL201 Safety and Tolerability



| Event | Number of Patients |
|-----------------------------|--------------------|
| Severe hypertension (SUSAR) | 1/12 |
| Mild hypertension | 3/12 |
| Injection Site Pain | 3/12 |
| Injection Site Reaction | 10/12 |
| Fatigue | 7/12 |
| Muscle cramps | 1/12 |
| Sinus Bradycardia | 1/12 |

- **1 SUSAR** reported of severe hypertension requiring overnight hospitalisation and medication to control, the patient remained on the trial at the same dose, with subsequent doses being preceded by prophylactic anti-hypertensive medication
- Although the patient had an established history of hypertension, the episodes were seen to be related to study drug administration
- All other possibly, probably or definitely related events listed in the table

VAL201 Expected Future

- Additional data analysis being conducted by Physiomics
 - This will provide further insight into the clinical data collected, future positioning of VAL201 and design of future clinical trials
- A partner or purchaser is sought to conduct and co-ordinate the **next clinical trial** – this trial should feature improved dosing regimens, as informed by pharmacokinetic profiles collected, and consider which stage of disease to target
- Next clinical trial expected to be a larger Phase 2 (or Phase 1/2) confirming and expanding current results
- Further analysis will highlight any noticeable **patient populations** or individual responders of note
- Further studies could be initiated in **other cancer types** as well as progressing prostate cancer

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