SUDA PHARMACEUTICALS LTD

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ASX Release

Anagrelide Project Update

- **A recent study supports SUDA's hypothesis that an anagrelide oral spray formulation may offer a safer alternative to the current commercial capsule to treat metastatic disease in patients with certain solid tumour cancers.**
- **Comparison of three new mouth spray formulations of anagrelide was made with the commercial capsule, Xagrid™.**
- **One of the novel formulations, SS-101, resulted in a statistically significant increase in bioavailability of the drug suggesting buccal absorption through the cheek.**
- **A comparatively smaller increase was seen in exposure to the cardiostimulatory metabolite.**
- **None of the formulations demonstrated any adverse effects on heart rate.**
- **None of the mouth spray formulations resulted in irritation in the oral cavity.**
- **Work is ongoing to create a pharmaceutical grade formulation.**

PERTH, AUSTRALIA – 22 September 2020: SUDA Pharmaceuticals Ltd (ASX: SUD), a leader in oro-mucosal drug delivery, is pleased to announce that it has now received the final report for a canine pharmacokinetic study recently completed at Covance Inc., Harrogate UK as previously announced on 27 May 2020.

Three carefully selected experimental oral spray formulations of anagrelide were compared with the commercial capsule form of the drug, Xagrid™. The objective of the study was to compare plasma levels of anagrelide and its cardiostimulatory metabolite following administration of the oral spray formulations with those after dosing with the capsule. The study enabled SUDA to test the hypothesis that an oral spray could provide a safer route of administration for anagrelide in treating metastatic disease in cancer patients by reducing exposure to the cardiostimulatory metabolite, 3-hydroxy anagrelide.

Formulation SS-101 displayed a statistically significant increase in bioavailability over the capsule of 43% (Figure 1). The other two formulations, EF-164 and EF-169, displayed a 27% increase and an 8% decrease in bioavailability over the capsule, respectively. Importantly, formulation SS-101 showed an increase of only 28% in exposure to the cardiostimulatory metabolite relative to the capsule formulation. According to Covance Inc., this provides evidence that a proportion of the drug from formulation SS-101 reaches the bloodstream by crossing the lining of the cheek.

The magnitude of the differential between the increase in bioavailability of the parent drug and the cardiostimulatory metabolite (43% of parent drug versus 28% of the metabolite) was unique to formulation SS-101 and suggests that a lower dose of anagrelide could be administered to cancer patients, which would result in a relative reduction in patient exposure to the cardiostimulatory intermediate.

Neither formulation EF-164 nor EF-169 showed the same level of increase in bioavailability, nor the same magnitude of difference between the parent drug and the cardiostimulatory metabolite.

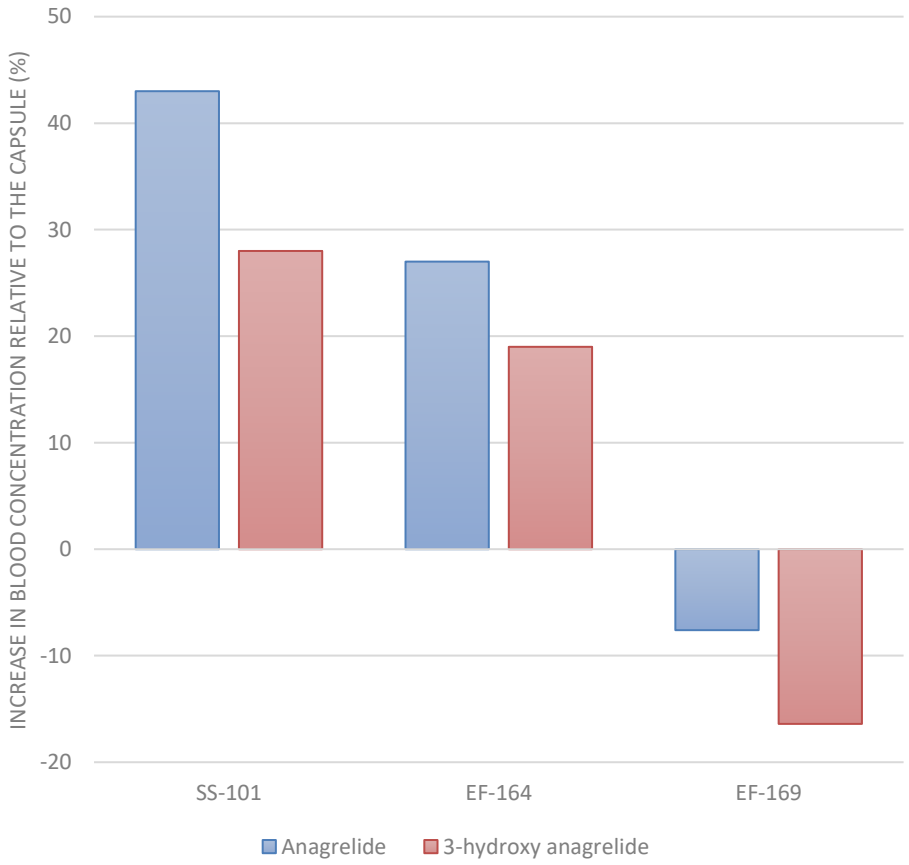

Figure 1. Relative systemic exposure (plasma levels) of anagrelide (blue) and its cardiostimulatory metabolite (red) from different mouth spray formulations (SS-101, EF-164 and EF-169). This shows that SS-101 resulted in higher concentrations of the drug in the blood stream than the commercially available capsule but a smaller increase in the cardiostimulatory intermediate, 3-hydroxy anagrelide.

As assessed by pulse rate, none of the formulations displayed cardiostimulatory effects. Upon visual assessment, no irritation of the oral mucosa was evident following administration of any of the oral spray formulations.

According to the project's director, Dr Richard Franklin, whose specialisms include drug metabolism and pharmacokinetic studies, and who was involved in the original development and registration of anagrelide for the treatment of Essential Thrombocythemia, "This is a very exciting development for the project. While we were hoping that all three of the oral spray formulations tested would have superior properties to the capsule form of the drug, we are delighted that one formulation in particular showed

evidence of buccal absorption, increased bioavailability and reduced exposure to the cardiostimulatory metabolite."

Why are these results important?

SUDA is developing anagrelide for the treatment of metastatic disease in patients who have certain solid tumour cancers. Clinical experience has shown that increased platelet numbers associated with several solid tumour cancers decreases progression-free life expectancy. Furthermore, anagrelide not only advantageously lowers blood platelets but it has also been shown to inhibit cancer cell movement towards platelet-producing cells, megakaryocytes, principally found in the bone marrow but also the lung, two likely sites of metastases.

Anagrelide has already been approved for the treatment of Essential Thrombocythemia (ET), in which patients have elevated platelet numbers and are at risk of thrombosis. A limiting factor for the widespread use of anagrelide in cancer in its current capsule form is the production of a cardiostimulatory metabolite that is generated during first pass metabolism of the drug in the liver. SUDA has shown that using one of its novel oral spray formulations, a proportion of the drug reaches the blood stream by crossing the buccal membrane in the mouth, enabling increased levels of the drug to reach the blood stream directly, while reducing the relative exposure to the cardiostimulatory metabolite that is generated. This supports SUDA's hypothesis that such a novel formulation of anagrelide may serve as a safer way to treat metastatic disease in cancer patients.

Next Steps

SUDA will continue to optimise formulation SS-101 to ensure its stability and to produce a pharmaceutical grade product.

Once the final formulation has been established, SUDA intends to complete the required pre-clinical toxicology studies prior to initiating clinical trials. As the drug itself has previously been approved by both the FDA and the EMA for ET, it is anticipated that a reduced package of preclinical testing will be required for the development of an oral spray version of anagrelide.

General

As of 30 June 2020 and taking into account a recent capital raising, SUDA has a solid cash position of $4.9 million. The company will continue to use the funds to develop anagrelide. The company also notes that its operations and supply chain remain unaffected by the COVID-19 pandemic.

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Glossary

Bioavailability	The proportion of a drug or other substance which enters the circulation when introduced into the body and so is able elicit a biological effect.
Buccal Administration	Buccal administration is a topical route of administration by which drugs held or applied to the buccal area of the mouth diffuse through the oral mucosa and enter directly into the bloodstream.
Cardiostimulatory	Drugs that accelerate cardiac function by increasing heart rate and myocardial contractility, which increases cardiac output and arterial pressure.
First Pass Metabolism	The first pass effect is a phenomenon of drug metabolism whereby the concentration of a drug, specifically when administered as a tablet or capsule, is greatly reduced before it reaches the systemic circulation, usually in the liver or the gut wall.
Pharmacokinetic	The effect of the body on a drug, refers to the movement of drug into, through, and out of the body—the time course of its absorption, bioavailability, distribution, metabolism, and excretion.

NOTES TO EDITORS:

About SUDA Pharmaceuticals Ltd

SUDA Pharmaceuticals Ltd (ASX: SUD) is a drug delivery company focused on oro-mucosal administration, headquartered in Perth, Western Australia. The Company is developing low-risk oral sprays using its OroMist® technology to reformulate existing pharmaceuticals. The many potential benefits of administering drugs through the oral mucosa (i.e. cheeks, tongue, gums and palate) include ease of use, lower dosage, reduced side effects and faster response time. SUDA's product pipeline includes ZolpiMist™, a first-in-class oral spray of zolpidem tartrate for the treatment of short-term insomnia. ZolpiMist is approved by the TGA and is marketed in the USA. SUDA has rights to the product outside of the US and Canada. Other products in development include oral sprays for the treatment of migraine headache, motion sickness, drug resistant epilepsy and certain cancers.

For more information, visit www.sudapharma.com