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## **Aliskiren, the first effective oral renin inhibitor, provides sustained 24 hour blood pressure control in combination with angiotensin receptor blocker**

### **Optimizing the inhibition of the Renin-Angiotensin-System**

**Basel/Switzerland and Bridgewater NJ/USA, 15 November 2005**

Speedel (SWX: SPPN) announced today newly-released results from its Phase II clinical research program demonstrating the benefits of aliskiren (SPP100), the first orally effective renin inhibitor, in the treatment of hypertension. Results from the Phase II trial conducted by Speedel were presented today at the American Heart Association Scientific Sessions 2005 in Dallas, Texas<sup>1</sup>. This study examined the safety, tolerability and effectiveness of lowering blood pressure (BP) by combining aliskiren with an angiotensin receptor blocker.

Results of the 9-week clinical study show that aliskiren provided patients with significantly greater night-time ambulatory BP measurement reductions (ABPM; continuous blood pressure monitoring) when added to irbesartan, an angiotensin receptor blocker (ARB) ( $p < 0.05$ ). In addition to its greater BP control, aliskiren neutralized the ARB-induced compensatory rise in Plasma Renin Activity (PRA), a risk factor for end organ damage.<sup>2,3</sup>

**Dr. J. Chris Jensen, Director of Pharmacology at Speedel**, commented: "These encouraging results further demonstrate aliskiren's effectiveness in lowering blood pressure over 24-hours, either as monotherapy or in combination with other treatments for hypertension. Aliskiren provides the potential additional benefit for patients of protecting the heart and kidneys."

Aliskiren (SPP100) is partnered with Novartis for Phase III development and commercialisation in hypertension with filing for registration in the USA expected in early 2006. Speedel is also working on several programs to create a new generation of renin inhibitors including SPP635 in Phase I, the SPP800 series and others in pre-clinical development.

#### **More on the clinical study<sup>1</sup>**

The open-label pilot study involved 23 patients with mild-to-moderate hypertension. All patients received once-daily treatment with irbesartan 150mg for 3 weeks, followed by irbesartan 150mg and aliskiren 75mg for 3 weeks, followed by irbesartan 150mg and aliskiren 150mg for 3 weeks. Twenty-four hour ABPM and PRA assays were performed at baseline and at the end of each period. The variables measured were: change from baseline in daytime systolic and diastolic ABPM; change from baseline in night-time systolic and diastolic ABPM; and change in PRA.

Irbesartan 150mg was administered throughout this trial first as monotherapy then in combination. The study results were:

- As monotherapy, irbesartan lowered ABPM throughout the 24-hour period.
- The addition of aliskiren 150mg to irbesartan provided significantly greater reductions in night-time systolic and diastolic ABPM ( $-13.2 \pm 2.7$  and  $-7.2 \pm 1.9$  respectively) compared with irbesartan monotherapy ( $p < 0.05$ ).
- A trend towards increased BP lowering with aliskiren and irbesartan in combination, compared with irbesartan monotherapy, was observed for daytime systolic and diastolic ABPM. These differences were not statistically significant, probably due to the small number of patients enrolled in this pilot study.
- Irbesartan 150 mg significantly increased PRA by 2.4-fold compared with baseline ( $p < 0.001$ ).
- The addition of aliskiren 75mg or 150mg to irbesartan 150 mg significantly reduced the compensatory rise in PRA stimulated by irbesartan monotherapy ( $p < 0.001$ ).

### The relevance of PRA

PRA is directly and independently associated with the occurrence of cardiovascular and renal disease among hypertensive patients such as heart<sup>2</sup> and kidney<sup>3</sup> damage ('end organ damage'). Despite their antihypertensive effects, some BP therapies increase the activity of renin.<sup>1</sup> Thus there is a need for new antihypertensive treatments that can reduce renin activity.<sup>4</sup>

### About Hypertension and Renin Inhibitors

Hypertension is a common disorder in which blood pressure is abnormally high, placing undue stress on the heart, blood vessels and other organs such as the kidney and the brain. Blood pressure is determined in two phases as the heart contracts and relaxes. Systolic blood pressure represents the force that blood exerts on the walls of arteries as the heart contracts to pump out blood. Diastolic blood pressure represents the force as the heart relaxes to allow the blood to flow into the heart.

Due to its wide prevalence and impact on cardiovascular health, hypertension is a major cause of disease and death in Europe and North America. More than one in three Europeans and North Americans over the age of 35 suffers from hypertension – but for the vast majority of patients who undergo hypertension treatment, the causes of high blood pressure are unknown. More than 40% of patients undergoing treatment with current therapies do not reach targeted blood pressure levels, and so there is a considerable unmet medical need. Global antihypertensive drugs sales are forecasted by Datamonitor to grow from USD 42 billion in 2004 to over USD 50 billion by 2009.

The latest potential therapeutic agents for hypertension are renin inhibitors. Renin is an enzyme produced in the kidneys in response to reduced renal perfusion. Through a cascade of biological events, renin acts to bring about sodium retention, an increase in blood pressure, and restoration of renal perfusion, which shuts off the signal for renin release. For hypertensive individuals, renin inhibitors are currently being investigated as a therapy that may provide benefits over current therapies to reduce blood pressure, decrease salt retention and may protect end organs such as the kidney, heart and brain.

Inhibition of renin, articulated as Plasma Renin Activity (PRA), is believed to be very important in end-organ protection (e.g. heart and kidney). PRA is an independent and surrogate marker for several cardio-renal diseases, such as myocardial infarction and chronic renal disease. It is only a Renin Inhibitor that lowers PRA efficiently, whereas most current leading antihypertensive drug classes such as ACEIs and ARBs increase PRA levels.

### References

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3. Baldoncini R, Desideri G, Bellini C et al. High plasma renin activity is combined with elevated urinary albumin excretion in essential hypertensive patients. *Kidney Int* 1999;56:1499–504.
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## About Speedel

Speedel is a biopharmaceutical company that seeks to create value for patients, partners and investors by developing innovative therapies for cardiovascular and metabolic diseases. Speedel is a world leader in renin inhibition, a promising new approach with significant potential for treating cardiovascular diseases. Our lead compound SPP100 (Aliskiren), the first-in-class renin inhibitor, is partnered with Novartis for Phase III development and commercialisation in hypertension with filing for registration expected in 2006. Our pipeline covers three different modes of action, and in addition to SPP100, includes SPP301 in Phase III, SPP200 in Phase II, SPP635 in Phase I, and several pre-clinical projects.

Speedel develops novel product candidates through focused innovation and smart drug development from lead identification to the end of Phase II. We either partner with big pharma for Phase III and commercialisation in primary-care indications, or we may ourselves complete Phase III development in specialist indications. Candidate compounds for development and the company's intellectual property come from our late-stage research unit Speedel Experimenta and from in-licensing.

Our team of approximately 70 employees, including over 30 experienced pharmaceutical scientists, is located at our headquarters and laboratories in Basel, Switzerland and at offices in New Jersey, USA and Tokyo, Japan. Since being founded in 1998, we have raised gross proceeds of CHF 239 million (approximately EUR 154 million or USD 191 million) from private placements of equity securities and two convertible loans and we have had total revenues, principally from milestone payments, of CHF 57.7 million (approximately EUR 37 million or USD 46 million). The company's shares were listed on the SWX Swiss Exchange under the symbol SPPN on 08 September 2005.

## Forward looking statements

This press release includes forward-looking statements that involve substantial risks and uncertainties. These forward-looking statements are based on our current expectations and projections about future events. All statements, other than statements of historical facts, regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The word "may" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations described in these forward-looking statements and you should not place undue reliance on them. There can be no assurance that actual results of our research and development activities and our results of operations will not differ materially from these expectations. Factors that could cause actual results to differ from expectations include, among others: our or our partners' ability to develop safe and efficacious products; our or our partners' ability to achieve positive results in clinical trials; our or our partners' ability to obtain marketing approval and market acceptance for our product candidates; our ability to enter into future collaboration and licensing agreements; the impact of competition and technological change; existing and future regulations affecting our business; changes in governmental oversight of pharmaceutical product development; the future scope of our patent coverage or that of third parties; the effects of any future litigation; general economic and business conditions, both internationally and within our industry, including exchange rate variations; and our future financing plans.

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