



**AM-112: A β -lactamase inhibitor for
antibiotic combination products**

Information Summary

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1. Executive summary

Amura Therapeutics Limited ("Amura") exclusively owns the commercial and intellectual property rights to a novel family of oxapenem β -lactamase inhibitors ("BLIs") and these products are offered as high quality licensing opportunities ready to advance to clinical trials. Oxapenems exhibit antibacterial activity and, more importantly, potent broad-spectrum inhibitory activity against Class A, C and D β -lactamases. The exciting potential of oxapenem BLI's has been recognised for over 20 years, but clinical development has been prevented primarily by low chemical stability. Amura has solved the chemical stability issue through the identification of a sub-family of oxapenems, the 'zwitterionics' that provide the breakthrough to materials with significantly improved stability. **AM-112**, a zwitterionic oxapenem, is the lead candidate in late pre-clinical development and given the appropriate investment will be ready for Phase I assessment in approximately 12-months. Therapeutically, **AM-112** has shown significant promise in combination with β -lactam antibiotics such as penicillins and cephalosporins, providing products that exhibit a substantially improved spectrum of activity when compared to the β -lactams *per se*. **AM-112** is ideally suited for *i.v.* administration compatible with a hospital setting, targeting infections in the fastest growing segment of the \$30 billion *per year* antibiotics market. Commercially, such combinations offer new business and intellectual property opportunities with both emerging antibiotics and with successfully established, but off-patent, compounds that are otherwise open to generic competition.

The comprehensive pre-clinical package compiled for **AM-112** has made significant progress over the last 2 years and now includes extensive *in vitro* and *in vivo* microbiology, toxicology, a scalable chemical synthesis, and establishment of broad ranging granted intellectual property rights. Notable highlights include;

(i) CHEMISTRY

- Process for production of high purity crystalline compounds established, suitable for adaptation to multi-kilo GMP synthesis.

(ii) MICROBIOLOGY

- Potent inhibitor of Class A, C, D and extended spectrum β -lactamases (ESBLs), broader spectrum than clavulanic acid (Augmentin, annual sales >£1billion) and tazobactam (Tazobactam, annual sales >\$750 million).
- Activity confirmed *in vitro* and *in vivo* against highly resistant bacterial isolates
- Potential to form potent, β -lactamase stable, combination products with cephalosporins and penicillins.

(iii) TOXICOLOGY

- Clean preliminary safety pharmacology profile e.g. low hERG binding, cytotoxicity assessment, CEREP diversity screen.
- 7-day repeat dose toxicology in mouse showed no adverse histopathological or clinical chemistry signs at 100mg/kg.

(iv) PHARMACOKINETICS (PK) / PHARMACODYNAMICS (PD)

- Pharmacokinetic data in rodent with half life equivalent to many cephalosporins e.g. ceftazidime.
- PD models demonstrate potential for once-a-day dosing regimen

(iii) INTELLECTUAL PROPERTY

- Strong, durable and exclusive worldwide IP position to 2022.
 - The 'zwitterionic' sub-family provide the breakthrough to more stable materials.
- Selections covering the lead analogue **AM-112** have been granted in Australia, Canada, China, Europe, India, Japan, South Korea, Mexico, US and are under examination in the remaining territories.

(iv) COMMERCIAL OPPORTUNITY

- **AM-112** / β -lactam combinations offer the potential for development of next generation broad spectrum antibiotic preparations, extending the scope of the established market leaders such as Augmentin (amoxicillin/clavulanate) and Tazocin (piperacillin/tazobactam).
 - e.g. a combination of **AM-112** with *i.v.* infused ceftriaxone (Rocephin), a very effective once daily β -lactam, may offer the exciting potential for the first once daily combination product.
- New intellectual property opportunities with both emerging antibiotics and with successfully established, but off-patent, compounds that are otherwise open to generic competition.

Amura is actively seeking out-licensing opportunities with globally-recognised licensing partners to develop its β -lactamase inhibitor portfolio, in particular AM-112.