Product Portfolio: Intravenous Anesthetics

Overview

Description	Propofol, midazolam, and etomidate are the most common intravenous anesthetics used in clinical applications today. Unfortunately, the drug formulations that are available on the market still show many disadvantages. Improved prodrugs and derivatives of the most common intravenous anesthetics were developed (LK-396, EL-0052, and EL-001) by the company we have collaborated with, which is engaged in the development of modified new drugs and innovative drug candidates. These anesthetics show better pharmacokinetics, significantly lower drug toxicity levels, and other advantages compared to current market leaders.
Pipeline	LK-396: water-soluble prodrug of propofol EL-0052: etomidate derivative EL-001: midazolam derivative
Drug Modality	Small molecule
Indication	Anesthesia
Status	Preclinical/Phase II (NMPA)
Patent	Granted

Licensing Opportunities

All three intravenous anesthetics programs (LK-396, EL-0052, and EL-001) are currently open for out-licensing opportunities worldwide.

Propofol Prodrug

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Drug Name	LK-396
Description	LK-396 overcomes the problem of poor water solubility of propofol, thus avoiding the stimulation at drug's injection site, caused by the release of propofol from fat emulsion. Compared with another prodrug - propofol phosphate, LK-396 shows significantly better pharmacokinetics and no formaldehyde release *in vivo*. LK-396 has a high therapeutic index, thus it is a safe anesthetic product with huge market potential.
Target	$GABA_A$
Drug Modality	Small molecule
Indication	Anesthesia
Formulation	Freeze-dried powder injection/TBD
Product Category	Modified new drug
Mechanism of Action	Activation of the $GABA_A$ receptor complex
Status	Preclinical
Patent	Patents have been granted in the US and Europe.

Etomidate Derivative

Drug Name	EL-0052
Description	Etomidate is a suitable anesthetic for the elderly and critically ill patients, showing no or little effects on circulation and respiratory system. However, prolonged use of etomidate results corticosteroid synthesis inhibition, significantly increasing surgical mortality. EL-0052 not only avoids that, but also retains all the advantages of etomidate, thus ensuring safe anesthesia.
Target	$GABA_A$
Drug Modality	Small molecule
Indication	Anesthesia
Formulation	Intravenous emulsions
Product Category	Innovative drug
Mechanism of Action	Positive modulation of GABA-mediated activity and direct activation of $GABA_A$

	receptors
Status	Phase II (NMPA)
Patent	Patents have been granted in the US, Europe, and Japan.

Midazolam Derivative

Drug Name	EL-001
Description	A common midazolam derivative, remimazolam, usually can be toxic by producing genotoxic impurities while in storage, and by producing formaldehyde in patient's body. EL-001, an ethyl ester hydrochloride derivative of midazolam, does not show any similar toxicities. Animal studies have shown that EL-001 is more effective and has quicker onset of action. In addition, its duration of action and recovery time after withdrawal are both shorter than remimazolam, thus making EL-001 easier to control, and a much better option for the patients in general.
Target	$GABA_A$
Drug Modality	Small molecule
Indication	Anesthesia
Formulation	Freeze-dried powder injection/TBD
Product Category	Innovative drug
Mechanism of Action	$GABA_A$ BZ site receptor agonist
Status	Preclinical
Patent	Patents have been granted in the US and Europe, and international patents under PCT are pending.

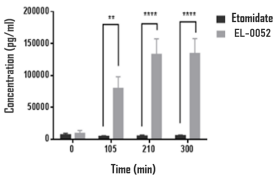
Data

Effects of EL-0052 and Etomidate on Corticosteroid Secretion Inhibition in Canine Model

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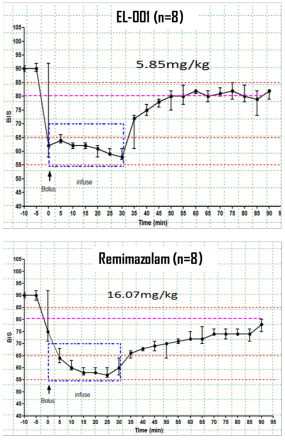
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ACTH (1-24) was administered to stimulate corticosterone secretion in canine model. Corticosterone concentration in serum was then determined.

Results showed that corticosterone concentration did not change in the etomidate group, both before and after the administration of ACTH (1-24). However, in the EL-0052 group corticosterone concentration increased significantly after ACTH (1-24) administration, and was higher compared to the etomidate group.



Bispectral Index Score Monitoring of EL-001 and Remimazolam in Rat Model

The bispectral index score (BIS) has been used as an indicator of a sedative state and is related to anesthetic agents and noxious stimulus. BIS was measured after the administration of EL-001 or remimazolam.

After bolus infusion, BIS decreased faster in rats administered with EL-001 than with remimazolam. Also, recovery of consciousness was significantly quicker in EL-001-treated rats.

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