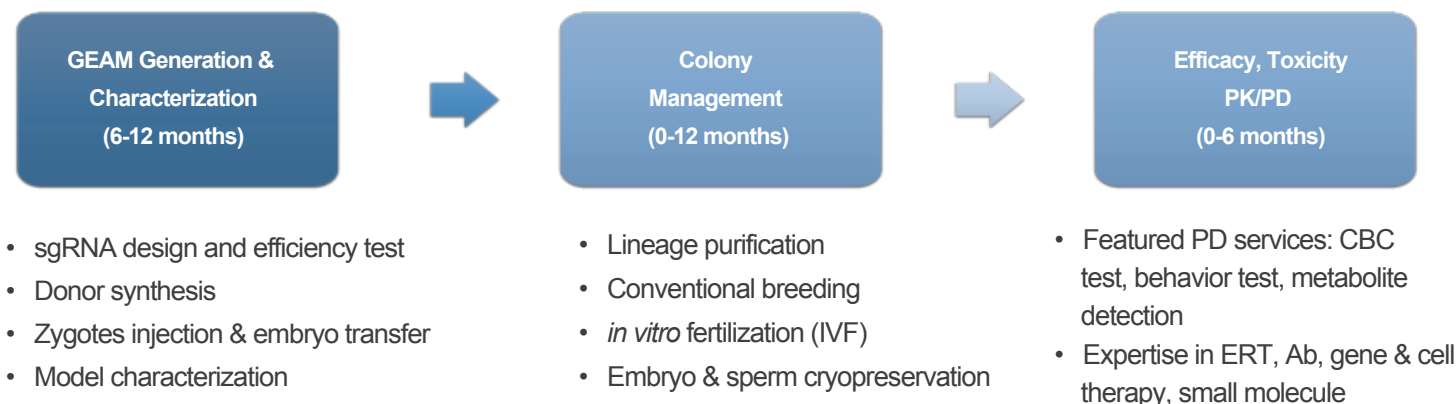**WuXi AppTec** 药明康德

Rare genetic disease platform

- **From the generation and characterization of genetically engineered animal model (GEAM) to colony management and pre-clinical pharmacology research**
- **A wide range of diseases, including hematologic, metabolic, neurologic and immunologic diseases**

From GEAM generation to pharmacology

GEAM Generation & Characterization (6-12 months)	→	Colony Management (0-12 months)	→	Efficacy, Toxicity PK/PD (0-6 months)

- sgRNA design and efficiency test
- Donor synthesis
- Zygotes injection & embryo transfer
- Model characterization

- Lineage purification
- Conventional breeding
- in vitro fertilization (IVF)
- Embryo & sperm cryopreservation

- Featured PD services: CBC test, behavior test, metabolite detection
- Expertise in ERT, Ab, gene & cell therapy, small molecule

In-house collection of GEAMs in KO/KI mouse & rat

21	36	13	12	17
hematology	metabolism	neurology	immunology	Others

Behavioral assessment platform

Contact us
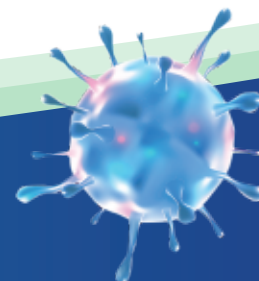
Equipment for embryonic operation and *in vitro* testing

Stereoscopic Microscope
embryonic operation

Microscopic Operating System
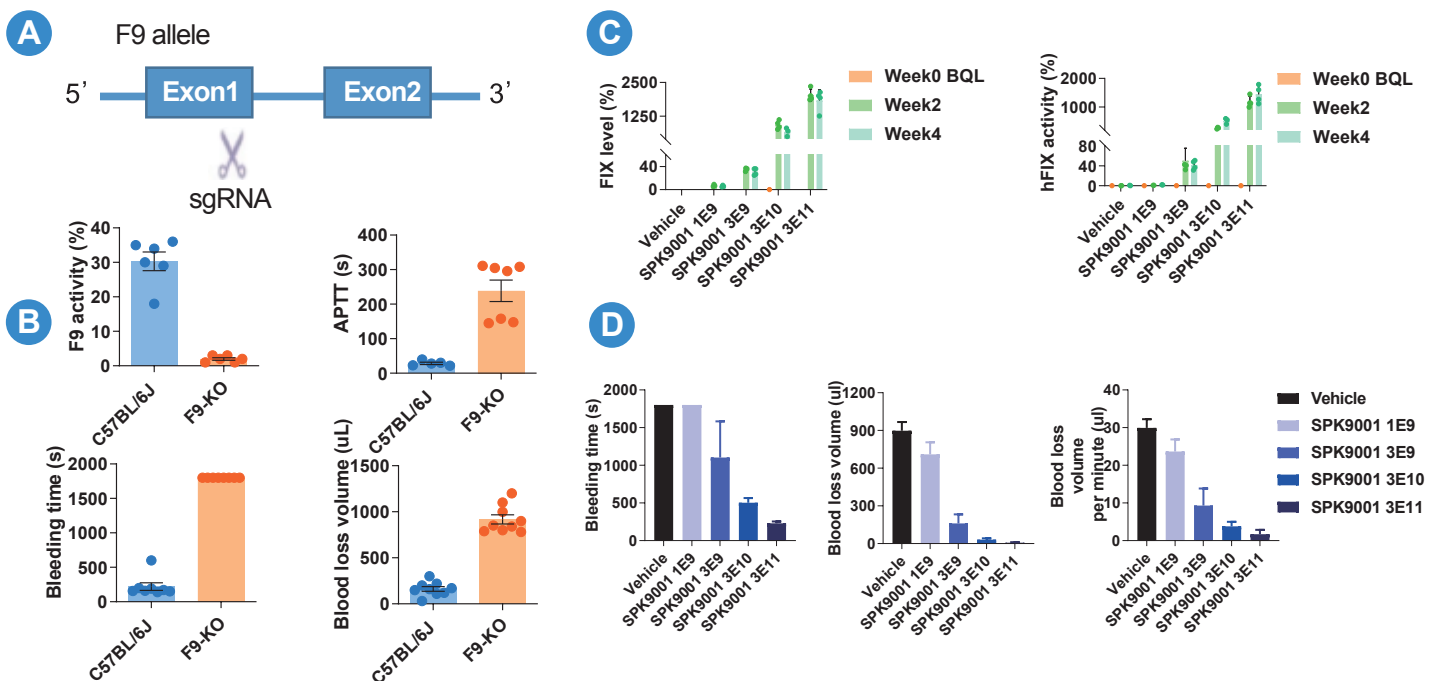Microinjection & embryonic operation

Bio-Rad Gene Pulser Xcell
Nucleotides, DNA and RNA
electro-transfer

1300 MESO® QuickPlex SQ120
Multifactorial detection

**Animal Five-category
Hematology Analyzer**
Hemanalysis in animal blood

Case study: gene therapy in F9-KO hemophilia B model

A F9 allele

5' Exon1 — Exon2 3'

sgRNA

B
F9 activity (%) — C57BL/6J, F9-KO
APTT (s) — C57BL/6J, F9-KO
Bleeding time (s) — C57BL/6J, F9-KO
Blood loss volume (uL) — C57BL/6J, F9-KO

C
FIX level (%) — Vehicle, SPK9001 1E9, SPK9001 3E9, SPK9001 3E10, SPK9001 3E11 — Week0 BQL, Week2, Week4
hFIX activity (%) — Vehicle, SPK9001 1E9, SPK9001 3E9, SPK9001 3E10, SPK9001 3E11 — Week0 BQL, Week2, Week4

D
Bleeding time (s) — Vehicle, SPK9001 1E9, SPK9001 3E9, SPK9001 3E10, SPK9001 3E11
Blood loss volume (ul) — Vehicle, SPK9001 1E9, SPK9001 3E9, SPK9001 3E10, SPK9001 3E11
Blood loss volume per minute (ul) — Vehicle, SPK9001 1E9, SPK9001 3E9, SPK9001 3E10, SPK9001 3E11

Legend: Vehicle, SPK9001 1E9, SPK9001 3E9, SPK9001 3E10, SPK9001 3E11

F9-KO Haemophilia B murine model generation, characterization and validation. (A) Construction strategy of F9-KO mouse model. (B) Decreased plasma F9 activity, increased APTT, and impaired hemostasis in F9-KO mice. (C-D) Reversed phenotypes in F9-KO mice after AAV-F9 treatment, increased F9 level and activity (C), and improved hemostasis (D).