

主な開発品の治験概要

2018年12月31日現在

本資料の内容は表紙に記載した時点における情報です。治験の進捗に伴い、治験データベース上の公開情報は随時更新されます。弊社が実施中の治験に関する最新情報につきましては、以下URLをご参照ください。

<https://clinicaltrials.gov/>

<https://www.clinicaltrials.jp/>

弊社の開発パイプラインの全体像は、以下URLよりご覧いただけます。

https://www.kyowa-kirin.co.jp/research_development_production/pipeline/index.html

List of abbreviations

AE	Adverse Events
DLT	Dose Limiting Toxicity
GFR	Glomerular Filtration Rate
iv	Intravenous
MTD	Maximum Tolerated Dose
ORR	Overall Response Rate
PD	Pharmacodynamics
PFS	Progression Free Survival
PK	Pharmacokinetics
po	Peroral
Q2W	Every Two Weeks
Q4W	Every Four Weeks
Q12W	Every Twelve Weeks
QD	Once Daily
QW	Once Weekly
sc	Subcutaneous

Late-stage pipeline summary

KYOWA KIRIN

Phase II	Phase III
AMG531 (romiplostim) Aplastic Anemia	AMG531 (romiplostim) Aplastic Anemia
ASKP1240 (bleselumab) Recurrence of focal segmental glomerulosclerosis in de novo kidney transplant recipients	KHK4827 (brodalumab) axSpA
KHK2375 (entinostat) Breast cancer	KHK7580 (evocalcet) Primary hyperparathyroidism
KHK4083 Ulcerative colitis	KRN23 (burosumab) XLH (pediatric)
KHK4083 Atopic Dermatitis	KW-0761 (mogamulizumab) CTCL
KRN23 (burosumab) TIO/ENS	KW-0761 (mogamulizumab) HAM
KRN23 (burosumab) XLH (pediatric)	RTA 402 (bardoxolone methyl) Diabetic Kidney Disease

KW-0761 (mogamulizumab)

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Hematological cancer - relapsed/refractory CTCL

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT01728805	U.S., Europe, Japan, others	Dec-18 N=372	<u>Arm 1: KW-0761</u> •1.0 mg/kg QW x 4 in cycle 1 then Q2W until progression <u>Arm 2: Vorinostat</u> •400 mg, po, QD	•Primary endpoint: PFS •Secondary endpoint: ORR	

KW-0761 (mogamulizumab)

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Solid tumor

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I/II NCT02705105	U.S.	Oct-18 N=114	<u>KW-0761 + Nivolumab</u> <ul style="list-style-type: none">•Part 1 (Dose Escalation Phase) KW-0761 and nivolumab are administered (iv) in combination.•Part 2 (Expansion Phase) Patients will be treated with MTD established in Part 1	<ul style="list-style-type: none">•Primary endpoint: MTD, DLT•Secondary endpoint: Objective tumor response rate	Jointly developed with Bristol-Myers Squibb
Phase I NCT02476123	Japan	Oct-19 N=108	<u>KW-0761 + Nivolumab</u> <ul style="list-style-type: none">•Part 1 (Dose Escalation Phase) KW-0761 and Nivolumab are administered (iv) in combination•Part 2 (Expansion Phase) Patients will be treated with MTD established in Part 1	<ul style="list-style-type: none">•Primary endpoint: AE, DLT	Jointly developed with Ono Pharmaceutical / Bristol-Myers Squibb

KW-0761 (mogamulizumab)

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Solid tumor – cont.

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I NCT02867007	U.S.	Aug-19 N=50	<u>KW-0761 + KHK2455</u> •Part 1 (Dose Escalation Phase) KHK2455 monotherapy [Cycle 0] followed by KHK2455 + KW-0761 combination [Cycle 1] •Part 2 (Expansion Phase) Patients will be treated with the recommended dose of KHK2455 established in Part 1 in combination with KW-0761	•Primary endpoint: AE	

KW-0761 (mogamulizumab)

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HTLV-1 Associated Myelopathy (HAM)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT03191526	Japan	Dec-20 N=66	<u>Arm 1: KW-0761 Q12W</u> iv, 0.3mg/kg, double-blind, after that open study for 24 weeks <u>Arm 2: Placebo Q12W</u> iv, double-blind, after that open study for 24 weeks	<ul style="list-style-type: none">•Primary endpoint: Improvement in Osame's motor disability score•Secondary endpoint: HTLV-1 Proviral load in peripheral blood, Mean of twice 10 m walking time, Modified Ashworth Scale	

KRN23 (burosumab)

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XLH (pediatric)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02915705	North America, Europe, Australia, Japan, Korea	Sep-19 N=61	<u>Arm 1: KRN23</u> •sc, Q2W, 0.8 mg/kg starting dose <u>Arm 2: Control (Phosphate and Active Vitamin D)</u> •po, multiple daily doses •Extension period: KRN23, sc, Q2W, 0.8 mg/kg starting dose	•Primary endpoint: Improvement in rickets •Other endpoint: Change in Serum P, 1,25(OH) ₂ D (1,25-dihydroxyvitamin D), Growth, Six Minute Walk Test and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02750618	U.S.	Sep-19 N=13	<u>KRN23</u> •sc, Q2W, 160 weeks	•Primary endpoint: AE, PD •Other endpoint: Change in rickets, lower extremity skeletal abnormalities, recumbent length/standing height and so on	Jointly developed with Ultragenyx (U.S.)
Phase III NCT03233126	Japan	Dec-19 N=10	<u>KRN23</u> •sc, Q2W, 86 weeks	•Primary endpoint: AE •Secondary endpoint: Laboratory values, Change in Serum P, 1,25(OH) ₂ D (1,25-dihydroxyvitamin D), Rickets Severity Score (RSS) total score, Six Minute Walk Test, PK and so on	

KRN23 (burosumab)

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TIO/ENS

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02304367	U.S.	Dec-19 N=17	<u>KRN23</u> •sc, starting dose of 0.3 mg/kg, Q4W. Doses may be titrated up to a maximum of 2.0 mg/kg, Q2W.	•Primary endpoint: The proportion of subjects achieving mean serum P levels above the lower limit of normal, Percent change from baseline in excess osteoid based on analysis of iliac crest bone biopsies after 48 weeks of KRN23 treatment •Secondary endpoint: AE, PK, PD, bone turnover biomarkers (ex.BALP, CTx, P1NP), osteocalcin, BFI (Brief Fatigue Inventory), BPI and so on	Jointly developed with Ultragenyx (U.S.)
Phase II NCT02722798	Japan, Korea	Jun-19 N=6	<u>KRN23 Q4W</u> •sc, 44 weeks	•Primary endpoint: Serum P concentration •Secondary endpoint: PK, PD, Evaluate changes in skeletal disease/osteomalacia and so on	

KHK7580 (evocalcet)

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Primary hyperparathyroidism

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT03280264	Japan	Oct-19 N=10	<u>KHK7580</u> •po, 24 weeks	•Primary endpoint: Percentage of subjects whose corrected serum calcium level is maintained \leq 10.3 mg/dL for 2 weeks	

RTA 402 (bardoxolone methyl)

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Diabetic Kidney Disease

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III AYAME NCT03550443	Japan	Mar-22 N=700	<u>Arm 1: RTA 402</u> •5, 10, or 15 mg, po, QD <u>Arm 2: Placebo</u> •po, QD	•Primary endpoint: Time to onset of a $\geq 30\%$ decrease in eGFR (estimated GFR) from baseline or end-stage renal disease (ESRD)	

KHK2375 (entinostat)

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Breast cancer

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT03291886	Japan	Nov-21 N=124	<u>Arm 1 : KHK2375 + Exemestane</u> KHK2375: 5mg, po, QW Exemestane: 25mg, po, QD <u>Arm 2 : Placebo + Exemestane</u> Placebo: po, QW Exemestane: 25mg, po, QD	•Primary endpoint: PFS •Secondary endpoint: OS, Antitumor effect	

KHK4083

Ulcerative Colitis

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02647866	U.S. Europe, others	Nov-18 N=60	<u>Arm 1: KHK4083</u> <u>Arm 2: Placebo</u> •iv, multiple ascending doses from Baseline to Week 48	•Primary endpoint: AE, Improvement in the mucosa •Secondary endpoint: Antidrug antibody , Mucosal healing, mMES (modified Mayo endoscopy sub-score) and so on	

KHK4083

Atopic Dermatitis

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT03703102	North America, Europe, Japan,	Feb-21 N=250	<u>Arm 1: KHK4083</u> •sc, dose level 1, dosing regimen 2 <u>Arm 2: KHK4083</u> •sc, dose level 2, dosing regimen 1 <u>Arm 1: KHK4083</u> •sc, dose level 3, dosing regimen 1 <u>Arm 1: KHK4083</u> •sc, dose level 3, dosing regimen 2 <u>Arm 2: Placebo</u> •sc	•Primary endpoint: Percent change from baseline to Week 16 in EASI (Eczema Area and Severity Index) score	

KHK4827 (brodalumab)

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Axial Spondyloarthritis (axSpA)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02985983	Japan, Korea, Taiwan	Sep-19 N=120	<u>Arm 1: KHK4827</u> •sc, 16 weeks <u>Arm 2: Placebo</u> •sc, 16 weeks <u>Arm 1 and Arm 2 (from week 17 until week 66):</u> •sc, administered KHK4827	•Primary endpoint: Percentage of ASAS (Assessment of SpondyloArthritis international Society) 40 in axSpA subjects	

ASKP1240 (bleselumab)

KYOWA KIRIN

Recurrence of focal segmental glomerulosclerosis (FSGS) in de novo kidney transplant recipients

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02921789	U.S.	May-20 N=60	<u>Arm 1: ASKP1240</u> •Basiliximab + Methylprednisone + Prednisone + ASKP1240 + Tacrolimus <u>Arm 2 (Active Comparator): Standard of Care</u> •Basiliximab induction + Tacrolimus + Methylprednisone + Prednisone + MMF	•Primary endpoint: Recurrence of FSGS at 3 months post-transplant •Secondary endpoint: Recurrence of FSGS, BRAR, efficacy failure, and biopsy-proven rFSGS at 12 months post-transplant	Jointly developed with Astellas

AMG531 (romiplostim)

KYOWA KIRIN

Aplastic Anemia

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II/III NCT02773290	Japan, Korea	Dec-20 N=46	<u>AMG531</u> •sc, QW	•Primary endpoint: Proportion of subjects achieving a hematological response (any of the platelet response, erythroid response, and neutrophil response)	