

# **主な開発品の治験概要**

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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/>

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。

[http://www.kyowa-kirin.co.jp/research\\_development\\_production/pipeline/index.html](http://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
OS	Overall Survival
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	RTA 402 (bardoxolone methyl) Diabetic Kidney Disease
ASKP1240 (bleselumab) Recurrence of focal segmental glomerulosclerosis in de novo kidney transplant recipients	KHK4563 (benralizumab) Asthma	
KHK2375 (entinostat) Breast cancer	KHK4827 (brodalumab) Psoriasis	
KHK4083 Ulcerative colitis	KHK4827 (brodalumab) axSpA	
KRN23 (burosumab) TIO/ENS	KHK7580 (evocalcet) Primary hyperparathyroidism	
KRN23 (burosumab) XLH (pediatric)	KRN23 (burosumab) XLH (adult)	
KW-0761 (mogamulizumab) ATL	KRN23 (burosumab) XLH (pediatric)	
	KW-0761 (mogamulizumab) CTCL	
	KW-0761 (mogamulizumab) HAM	

# 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"><li>•Part 1 (Dose Escalation Phase) KW-0761 and nivolumab are administered (iv) in combination.</li><li>•Part 2 (Expansion Phase) Patients will be treated with MTD established in Part 1</li></ul>	<ul style="list-style-type: none"><li>•Primary endpoint: MTD, DLT</li><li>•Secondary endpoint: Objective tumor response rate</li></ul>	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"><li>•Part 1 (Dose Escalation Phase) KW-0761 and Nivolumab are administered (iv) in combination</li><li>•Part 2 (Expansion Phase) Patients will be treated with MTD established in Part 1</li></ul>	<ul style="list-style-type: none"><li>•Primary endpoint: AE, DLT</li></ul>	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"><li>•Primary endpoint: Improvement in Osame's motor disability score</li><li>•Secondary endpoint: HTLV-1 Proviral load in peripheral blood, Mean of twice 10 m walking time, Modified Ashworth Scale</li></ul>	



# KRN23 (burosumab)

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## XLH (adult)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02526160	U.S., Europe, Japan, Korea	Sep-18  N=134	<u>Arm 1: KRN23 Q4W</u> •sc, 1mg/kg, double-blind <u>Arm 2: Placebo Q4W</u> •sc, double-blind •cross over to receive KRN23 treatment at Week 24	•Primary endpoint: Proportion of subjects achieving mean serum P (phosphorus) levels above the lower limit of normal •Secondary endpoint: BPI (Brief Pain Inventory) Q3 Pain, PD, Bone biomarker and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase III NCT02537431	North America, Europe, Japan, Korea	Sep-18  N=14	<u>KRN23 Q4W</u> •1.0 mg/kg, 28 days, rounded to the nearest 10 mg up to a maximum dose of 90 mg	•Primary endpoint: O.Th (Osteoid Thickness), OS/BS (Osteoid surface/Bone surface), MLt (Mineralization lag time), OV/BV (Osteoid volume/Bone volume) •Secondary endpoint: Proportion of subjects achieving mean serum P levels above the lower limit of normal, MAR (mineral apposition rate), MS/BS (mineralizing surface), BFR (bone formation rate) and so on.	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02312687	U.S.	Nov-18  N=20	<u>KRN23 Q4W</u> •sc, 68 weeks (starting doses will be based on the subject's last dose in the previous study)	•Primary endpoint: AE •Secondary endpoint: Change from Baseline in serum FGF23, PD and so on	Jointly developed with Ultragenyx (U.S.)

# 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	Jun-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) <sub>2</sub> D (1,25-dihydroxyvitamin D), Growth, Six Minute Walk Test and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02163577	U.S., Europe	Sep-18 N=52	<u>Arm 1: KRN23 Q4W</u> <u>Arm 2: KRN23 Q2W</u> •sc, 64 weeks (16-week individual dose Titration Period, followed by a 48-week Treatment Period)	•Primary endpoint: Severity of rickets •Other endpoint: Change in Severity of Rickets, Growth, Walking Ability, Functional Disability and Pain and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02750618	U.S.	Oct-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.)

# KRN23 (burosumab)

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XLH (pediatric) – cont.

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
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) <sub>2</sub> 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.	Jun-19 N=17	<u>KRN23 Q4W</u> •sc, starting dose of 0.3 mg/kg (Week 0), 140 weeks	•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	<ul style="list-style-type: none"><li>•Primary endpoint: PFS</li><li>•Secondary endpoint: OS, Antitumor effect</li></ul>	

# 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	



# KHK4827 (brodalumab)

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## Psoriasis

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III  NCT02982005	Korea	Dec-18  N=60	<u>Arm 1: KHK4827</u> •sc, 12 weeks <u>Arm 2: Placebo</u> •sc, 12 weeks <u>Arm 1 and Arm 2 (from week 13 until week 62):</u> •sc, administered KHK4827	•Primary endpoint: PASI (Psoriasis area and severity index) 75 response, sPGA (Static physician's global assessment) 0 (clear) or 1 (almost clear)	

# 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)

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## 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)

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## 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)	