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Summary of late-stage clinical trials

As of Jun. 30, 2018

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The document contains information available on the date indicated in its cover page. The public information of clinicaltrials.gov is continuously updated as the trials make progress. See the current information on our ongoing trials at the Website.
https://clinicaltrials.gov/

The whole picture of our pipeline is available on the following website:
http://www.kyowa-kirin.com/research_and_development/pipeline/index.html

List of abbreviations

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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	Phamacokinetics
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

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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	Arm 1: KW-0761 •1.0 mg/kg QW x 4 in cycle 1 then Q2W until progression Arm 2: Vorinostat •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	KW-0761 + Nivolumab •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	•Primary endpoint: MTD, DLT •Secondary endpoint: Objective tumor response rate	Jointly developed with Bristol-Myers Squibb
Phase I NCT02476123	Japan	Oct-19 N=108	KW-0761 + Nivolumab •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	•Primary endpoint: AE, DLT	Jointly developed with Ono Pharma-ceutical / 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	KW-0761 + KHK2455 •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)

HTLV-1 Associated Myelopathy (HAM)

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Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT03191526	Japan	Dec-20 N=66	Arm 1: KW-0761 Q12W iv, 0.3mg/kg, double-blind, after that open study for 24 weeks Arm 2: Placebo Q12W Iv, double-blind, after that open study for 24 weeks	•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)

XLH (adult)

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Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02526160	U.S., Europe, Japan, Korea	Sep-18 N=134	Arm 1: KRN23 Q4W •sc, 1mg/kg, double-blind Arm 2: Placebo Q4W •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	KRN23 Q4W •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	KRN23 Q4W •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)

XLH (pediatric)

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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	Arm 1: KRN23 •sc, Q2W, 0.8 mg/kg starting dose Arm 2: Control (Phosphate and Active Vitamin D) •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, $1,25(OH)_2D$ (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	Arm 1: KRN23 Q4W Arm 2: KRN23 Q2W •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	KRN23 •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	KRN23 •sc, Q2W, 86 weeks	•Primary endpoint: AE •Secondary endpoint: Laboratory values, Change in Serum P, $1,25(OH)_2D$ (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	KRN23 Q4W •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	KRN23 Q4W •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	KHK7580 •po, 24 weeks	•Primary endpoint: Percentage of subjects whose corrected serum calcium level is maintained ≤ 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	Arm 1: RTA 402 •5, 10, or 15 mg, po, QD Arm 2: Placebo •po, QD	•Primary endpoint: Time to onset of a ≥ 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	Arm 1 : KHK2375 + Exemestane KHK2375: 5mg, po, QW Exemestane: 25mg, po, QD Arm 2 : Placebo + Exemestane Placebo: po, QW Exemestane: 25mg, po, QD	•Primary endpoint: PFS •Secondary endpoint: OS, Antitumor effect	

KHK4083

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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	Arm 1: KHK4083 Arm 2: Placebo •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	Arm 1: KHK4827 •sc, 12 weeks Arm 2: Placebo •sc, 12 weeks Arm 1 and Arm 2 (from week 13 until week 62): •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	Arm 1: KHK4827 •sc, 16 weeks Arm 2: Placebo •sc, 16 weeks Arm 1 and Arm 2 (from week 17 until week 66): •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	Arm 1: ASKP1240 •Basiliximab + Methylprednisone + Prednisone + ASKP1240 + Tacrolimus Arm 2 (Active Comparator): Standard of Care •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	AMG531 •sc, QW	•Primary endpoint: Proportion of subjects achieving a hematological response (any of the platelet response, erythroid response, and neutrophil response)	