Kyowa Kirin R&D Meeting 2023

December 11, 2023

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This document contains certain forward-looking statements relating to such items as the company's (including its domestic and overseas subsidiaries) forecasts, targets and plans. These forward-looking statements are based upon information available to the company at the present time and upon reasonable assumptions made by the company in making its forecasts, but the actual results in practice may differ substantially due to uncertain factors.

These uncertain factors include, but are not limited to, potential risks of the business activities in the pharmaceutical industry in Japan and overseas, intellectual property risks, risk of side effects, regulatory risks, product defect risks, risks of changes to the prices for raw materials, risks of changes to market prices, as well as risks of changes to foreign exchange rates and financial markets.

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Vision

Our Vision toward 2030

Kyowa Kirin will realize the successful creation and delivery of life-changing value that ultimately makes people smile, as a Japan-based Global Specialty Pharmaceutical company built on the diverse team of experts with shared passion for innovation.

* Make patients smile through dramatic improvements in quality of life by identifying the unmet medical needs of people battling with medical conditions and by creating and supplying new drugs or services that help them overcome those challenges.

Provide pharmaceuticals for unmet medical needs

We are focused on developing medicines for diseases where there is a clear patient need for new options. We make full use of multiple therapeutic modalities, including biotechnology such as antibody technology, and beyond, building on our Kyowa Kirin established strengths.

Address patient-centric healthcare needs

We will meet the needs of patients and society by providing value across the entire patient care pathway, delivering cutting-edge science and technology, grounded in our in-depth pharmaceutical knowledge and expertise.

Retain the trust of society

We pursue world-class product quality and operational excellence to grow our business in ways which build long-term trust with our stakeholders.

Research & Development Concept

Technology x Biology x OI

The Kyowa Kirin Group is aiming to build a competitive technology platform by enhancing and combining its drug discovery technologies and its drug discovery modalities.
By matching that technology platform with disease-oriented science and by harnessing open innovation with partners that have specific strengths, we aim to develop completely new technologies or select efficient drug discovery targets to create life-changing value.

Technology

We will continue to evolve our antibody technology, while also pursuing the possibilities of other modalities and building a platform that leads to innovative new therapies.

Disease Biology

Continue to provide “Only-one value drug” for UMN, while utilizing the disease science* cultivated to date within KKC

* Nephrology, Oncology, Immunology & allergy, CNS

Create Life-changing value with clear competitive advantages

Open Innovation (OI)

Continue to work on collaborative research activities* with academia, startups and other partners, combine this with rapid access to start up information gained from investment in VC funds and CVC funds, and tap into external innovation through advanced OI activities

* Reenergize the San Diego research base

The key drivers of our future growth

Global Strategic Products

CRYSVITA® burosumab

POTELIGEO® (mogamulizumab)

NOURIANZ® (istradefylline) tablets

Development Pipelines (Ph2 or later)

- rocatinlimab (atopic dermatitis)
- **KHK4951 nAMD** ★
- rocatinlimab (asthma)
  - Ph2 start schedule under consideration
- **KHK4951 DME** ★
  - Scheduled to start within 2023

Early-Stage Pipelines (Ph1 or earlier)

- KK4277
- REGULGENT™ ★
  - **KK2260** ★
  - **KK2269** ★
    - Scheduled to start in 2024Q1
- Other biologics

Note: Orchard Therapeutics plc's Pipelines

- OTL-200 (EU: Libmeldy®)
- OTL-203
- OTL-201

Today's agenda

- **Development Pipeline using REGULGENT™ - Our bispecific antibody technology**
  - About REGULGENT™
  - KK2260
  - KK2269
- **Toward the Successful Creation and Delivery of Life-changing Value**
  - KHK4951 (Ph1 study results and Ph2 studies overview)
  - Orchard Therapeutics plc (HSC-GT)

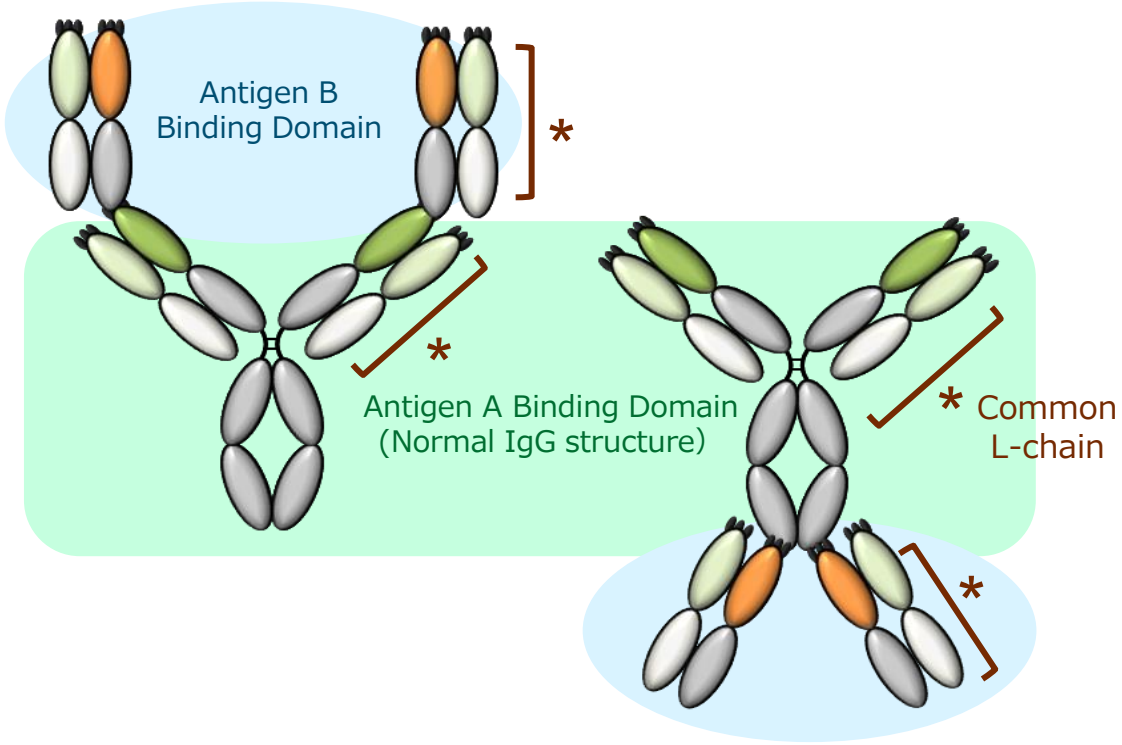
Development Pipeline using REGULGENT™
Our bispecific antibody technology

- **About REGULGENT™**
- KK2260
- KK2269

About REGULGENT™

General characteristics of bispecific antibodies
- Able to perform actions that IgG cannot by acting on two types of antigens*
- Composed of a combination of non-common L-chain antibodies or by utilizing antibody-like molecules

* e.g., cross-linking of two types of cells or molecules



N-terminal type C-terminal type

Characteristics of REGULGENT™

Simple structure, minimized immunogenicity
- Use of common L-chain (*), only natural IgG sequence
- Uniformity with no combination of different molecules
- Physical properties and pharmacokinetics equivalent to IgG

Bivalent-bivalent binding, N&C-terminal type
- Can be expanded to a variety of mechanisms of action

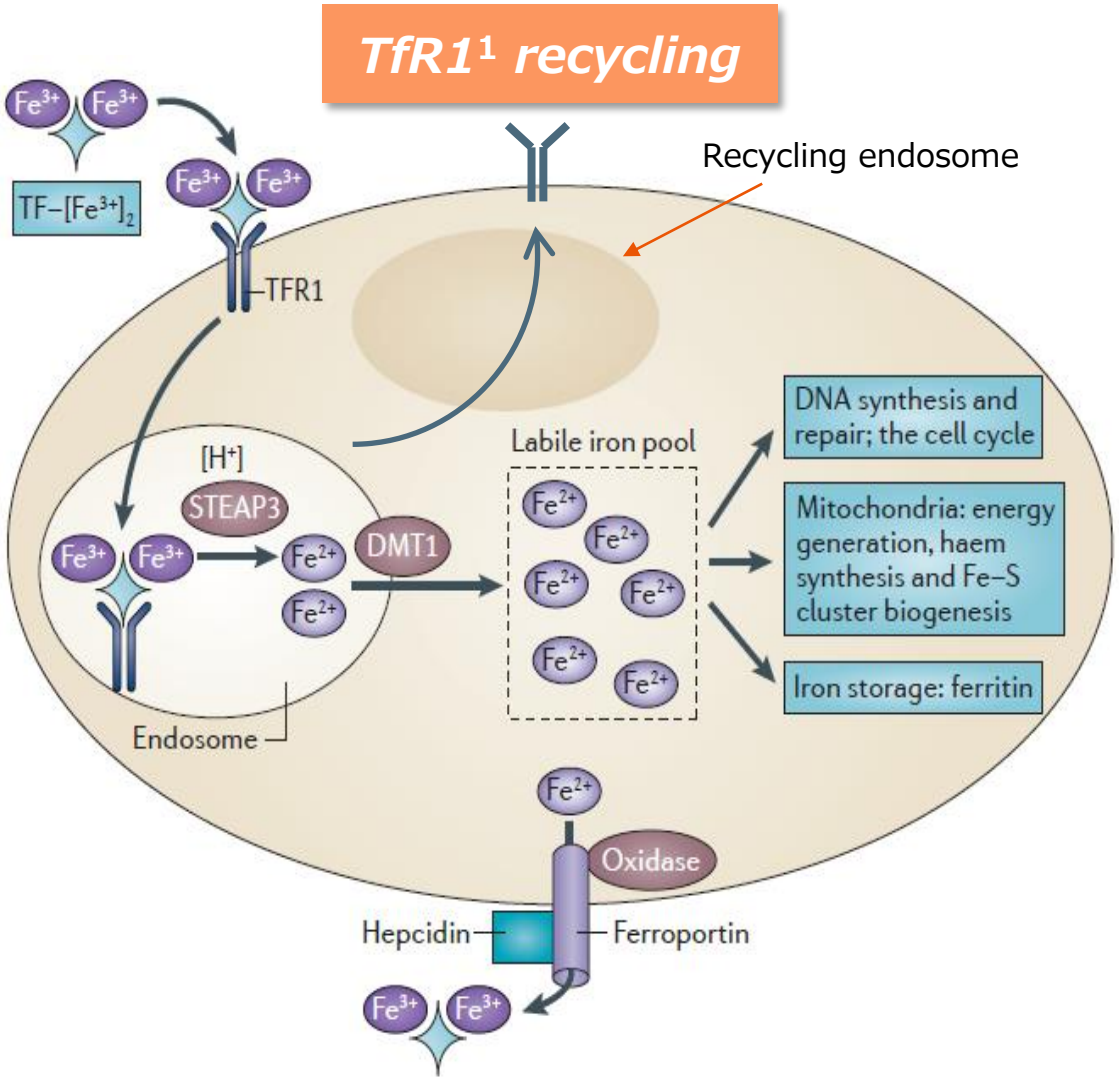
Stable production process, easy handling
- High productivity equivalent to IgG
- Can be adapted to the conventional antibody manufacturing process

Proprietary bispecific antibody technology created from our antibody R&D experience

Development Pipeline using REGULGENT™
Our bispecific antibody technology

- About REGULGENT™
- **KK2260**
- KK2269

Relationship between cells and iron



Modified from: Torti, S. V. et al., Nat Rev Cancer, 2013

Iron is an important element for cell growth and survival

- DNA synthesis

Ribonucleotide reductase - requires iron ions in the active center

- Energy generation

Iron ion is required for ATP production via TCA cycle[2] in mitochondria

TfR1 contributes to cellular uptake of iron

- Iron ions bind to transferrin, which binds to TfR1 and is taken up into the cell
- TfR1 is recycled after intracellular iron supply and is again involved in iron uptake

1. Transferrin receptor 1; 2. Tricarboxylic acid cycle = Citric acid cycle

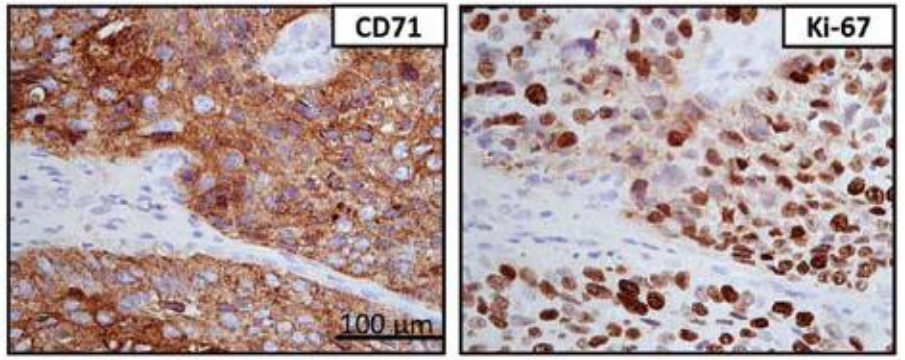
Relationship between cancers and iron

- Many cancer types have an association with iron

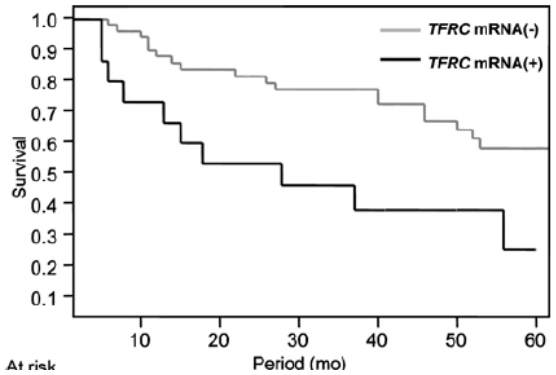
Type of cancer	Type of evidence
Non-small-cell lung cancer	Cell culture, animal models and epidemiological
Breast cancer	Cell culture, animal models, human tissue studies and epidemiological
Renal cell carcinoma	Cell culture and animal models
Hepatocellular cancer	Cell culture, animal models and epidemiological
Oesophageal, stomach, aerodigestive and gastric cancer	Human tissue studies, animal models and epidemiological
Colorectal cancer	Cell culture, human tissue studies, animal models and epidemiological
Prostate cancer	Cell culture and epidemiological
Haematological cancers (leukaemias, lymphomas and myeloma)	Cell culture, animal models, epidemiological and clinical case study
Melanoma	Cell culture and animal model
Pancreatic cancer	Cell culture, animal models and clinical trial
Bladder cancer	Cell culture

Torti, S. V. et al., Nat Rev Cancer, 2013

- High expression of TfR1 in many cancer types which affects cancer growth and prognosis



TfR1 expression of ESCC patient: Chan et al., *ONCOLOGY REPORTS,* 2014



Survival after surgery of ESCC patients: Wada et al., *Ann. Surg. Oncol.*, 2006

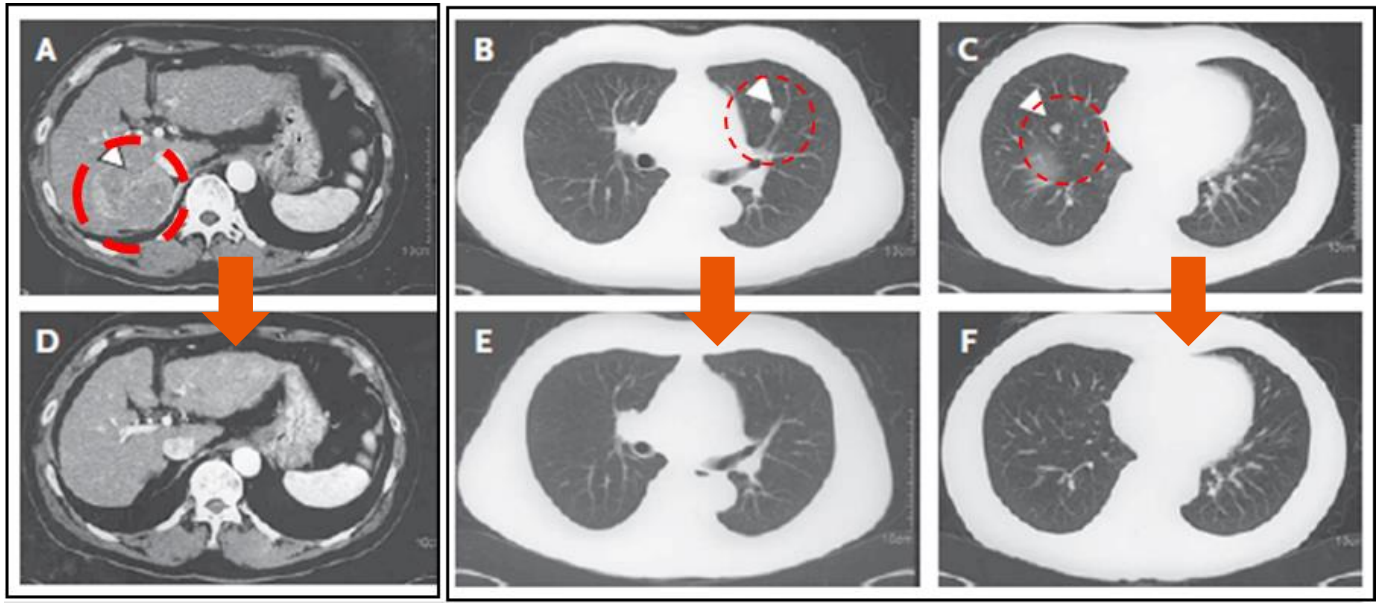
TfR1 = CD71: Transferrin receptor 1, Ki-67: One of the cell growth marker protein, ESCC: Esophageal squamous cell carcinoma

Anticancer effects and systemic side effects of iron depletion

- Efficacy of Deferoxiamine, an Iron Chelator, in Hepatocellular Carcinoma

Anticancer effect observed by iron depletion in cancer cells

Modified from: Yamasaki et al., N Engl J Med, 2011



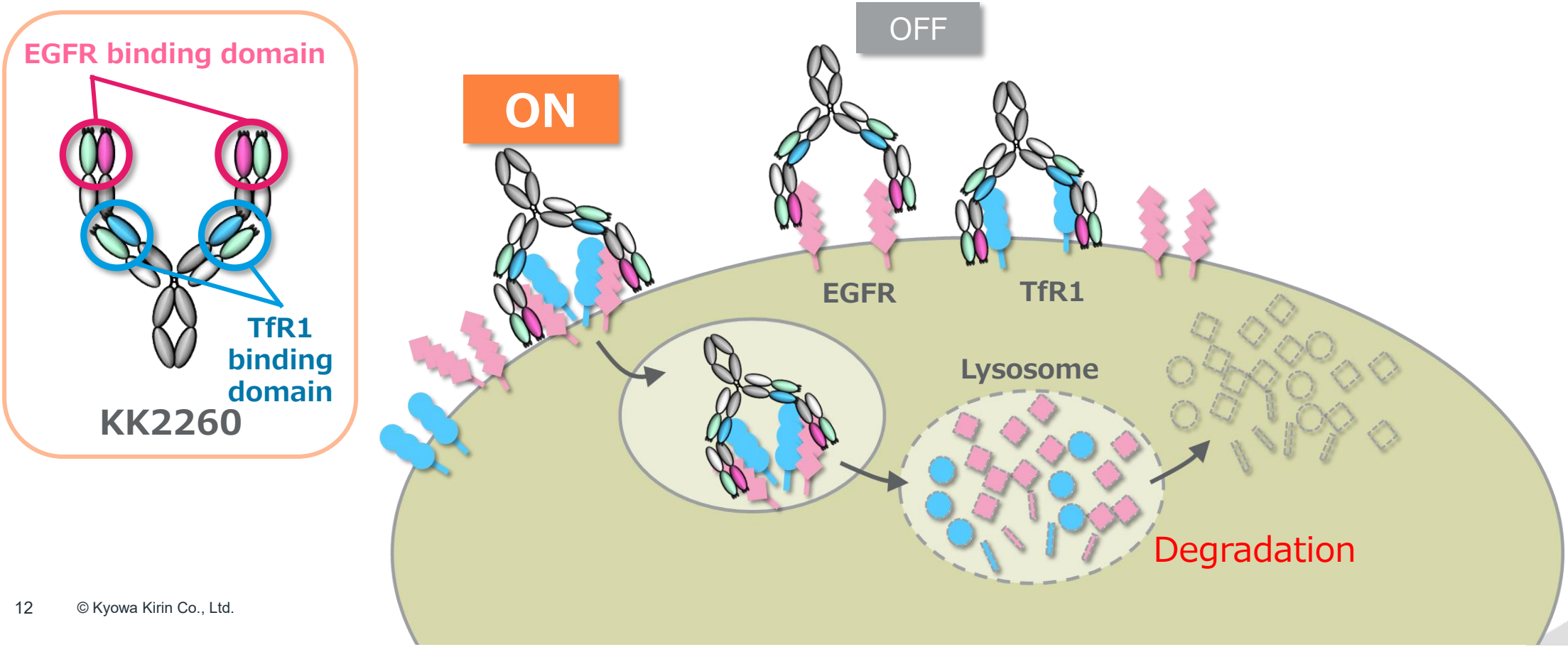
- However, systemic iron depletion raises a safety concern (e.g. severe anemia) because iron plays an important function in all cells

Need to find a way to suppress systemic side effects and exert only anticancer effects

KK2260: EGFR-TfR1 bispecific antibody

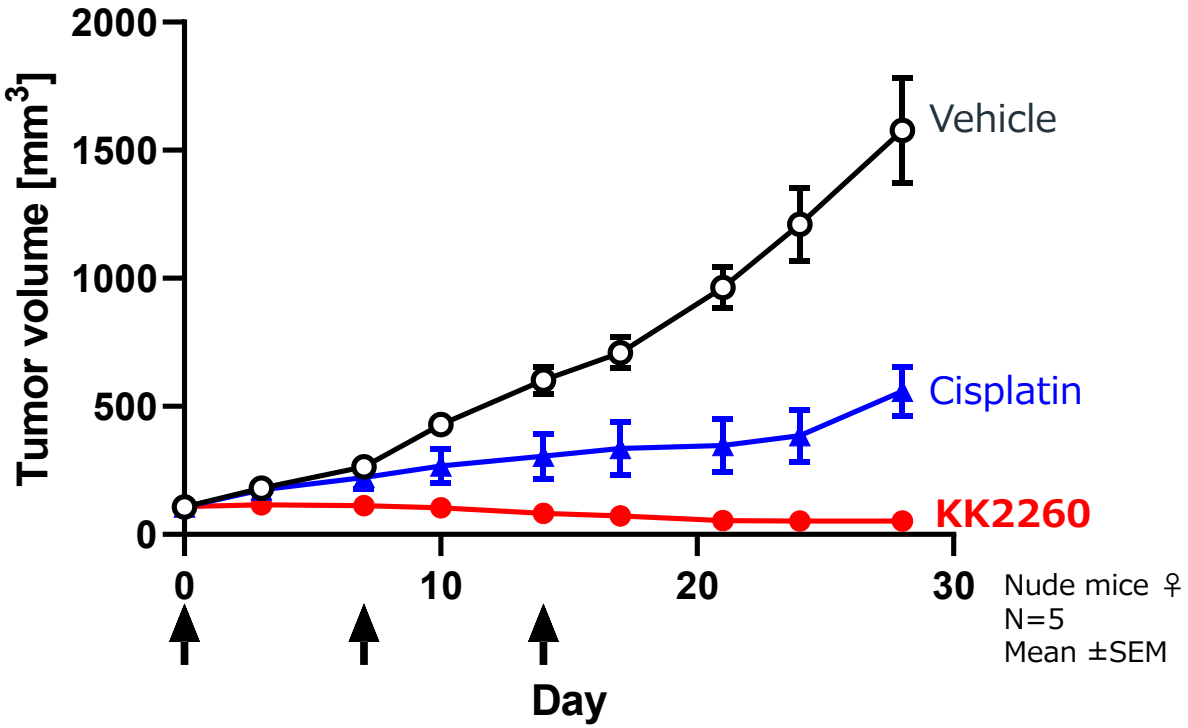
To avoid systemic side effects = selective iron depletion in cancer cells

- **No neutralizing activity when bound to TfR1 only or EGFR only**
- **Cross-links TfR1 and EGFR to induce TfR1 degradation in lysosomes**



KK2260: Drug Efficacy and Safety in Nonclinical Studies

Efficacy: ESCC[1] PDX[2] model (EGFR+/TfR1+)



High efficacy was shown in all three models evaluated

Safety

- **200 mg/kg of KK2260 was administered to cynomolgus monkeys once a week x 4 times**

  → No serious toxicity, including skin toxicity[3], was observed. Mild and transient anemia was observed.

In nonclinical studies, we found that KK2260 was able to exert its effects while suppressing systemic side effects.

Development for EGFR-high expressing cancers are planned.

1. Esophageal squamous cell carcinoma.
2. Patient-derived xenograft. ESCC PDX tumors were obtained from In-Vivo Science Inc.
3. Known as the side effect of EGFR neutralization

Development Pipeline using REGULGENT™
Our bispecific antibody technology

- About REGULGENT™
- KK2260
- **KK2269**

About CD40 agonistic antibody

Expectations

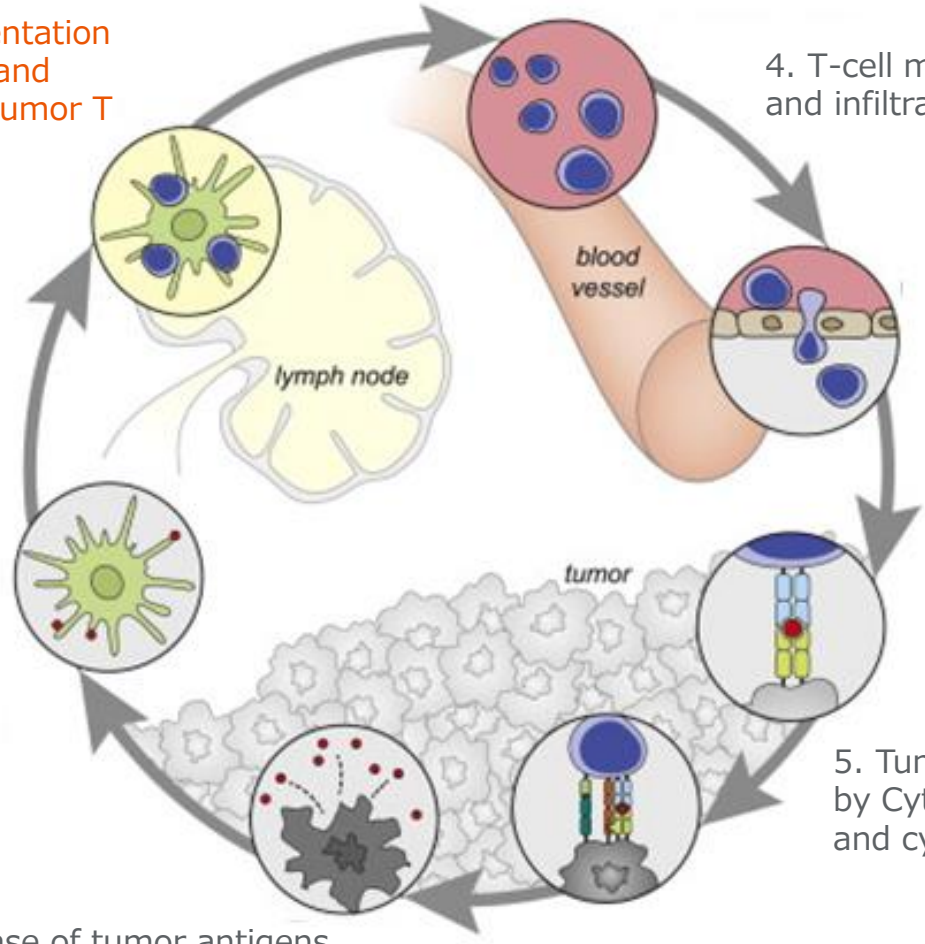
To cure cancer by inducing de novo anti-tumor immunity in patients that are not sufficiently aquaired anti-tumor immunity and/or that are refractory to existing immunotherapy

Issues

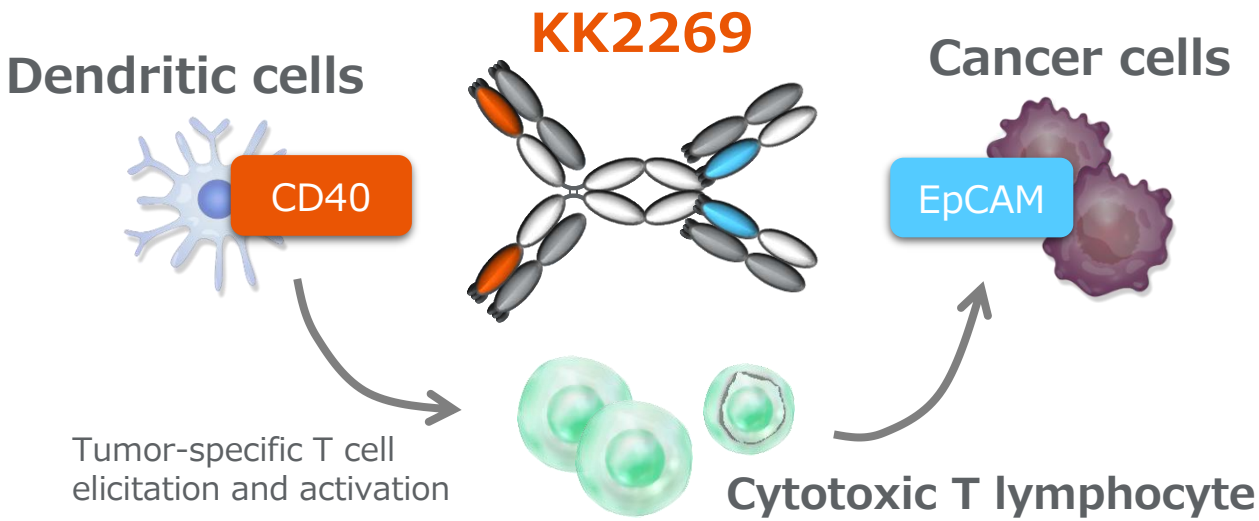
Over-activation of the systemic immune system, resulting in a narrow therapeutic window

Cancer Immunity Cycle

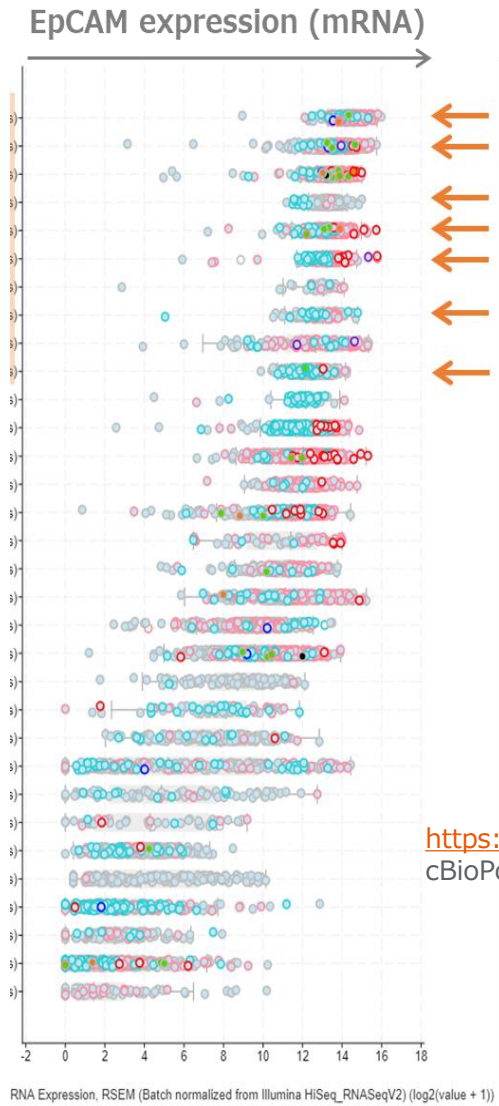
Modified from: *Immunity, Volume 39, Issue 1, 2013, 1–10*



KK2269: CD40-EpCAM* bispecific antibody



Examples of EpCAM-high expressing tumors



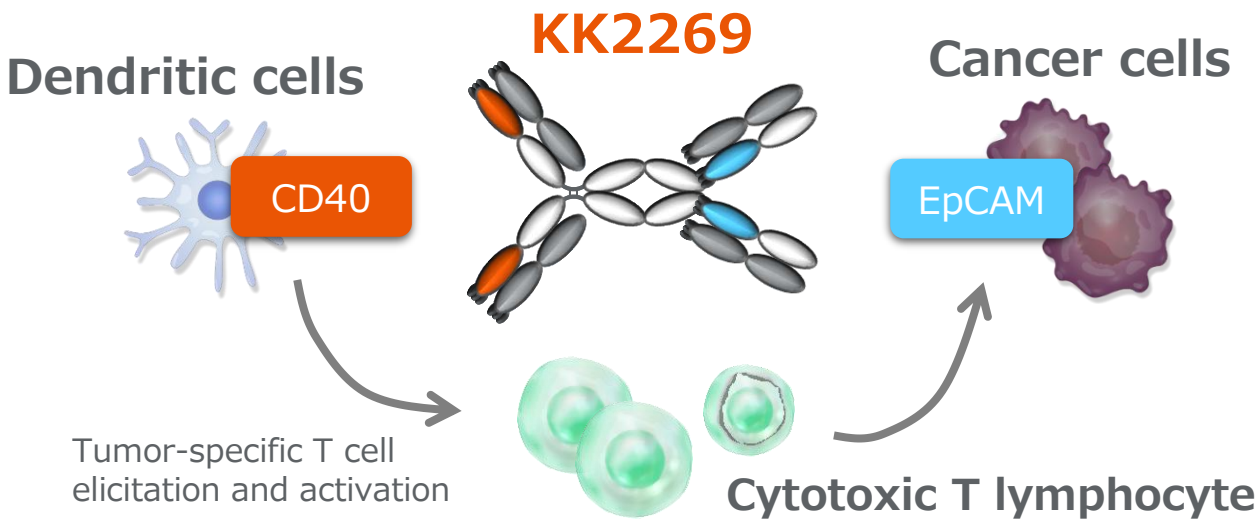
Underline:
Cancer types to be evaluated in Ph1

https://www.cbioportal.org/
cBioPortal

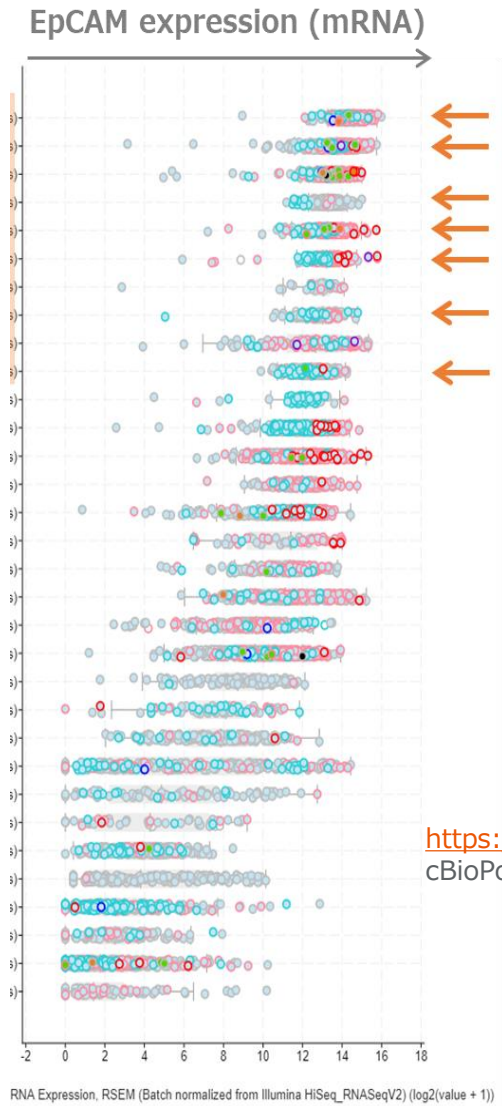
- **Targets CD40 and EpCAM simultaneously, exerting CD40 agonist activity against dendritic cells in close proximity to the tumor**
- **Successfully separated the induction of anti-tumor immunity from its side effects (systemic immune hyperactivation)**

*EpCAM: Epithelial Cell Adhesion Molecule, marker molecules for epithelial tumors

KK2269: CD40-EpCAM* bispecific antibody



Examples of EpCAM-high expressing tumors



Underline:
Cancer types to be evaluated in Ph1

https://www.cbioportal.org/
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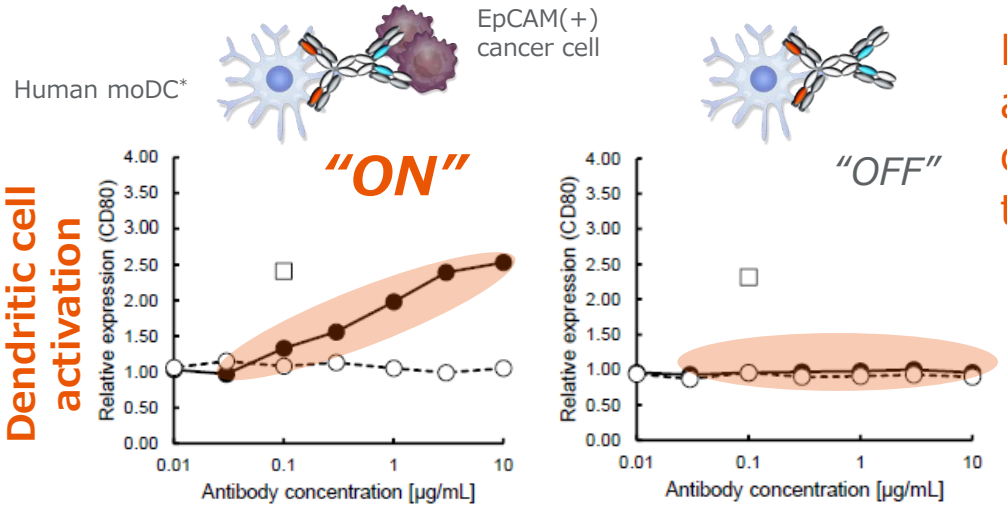


Function as a CD40 agonist only for dendritic cells in close proximity to the cancer

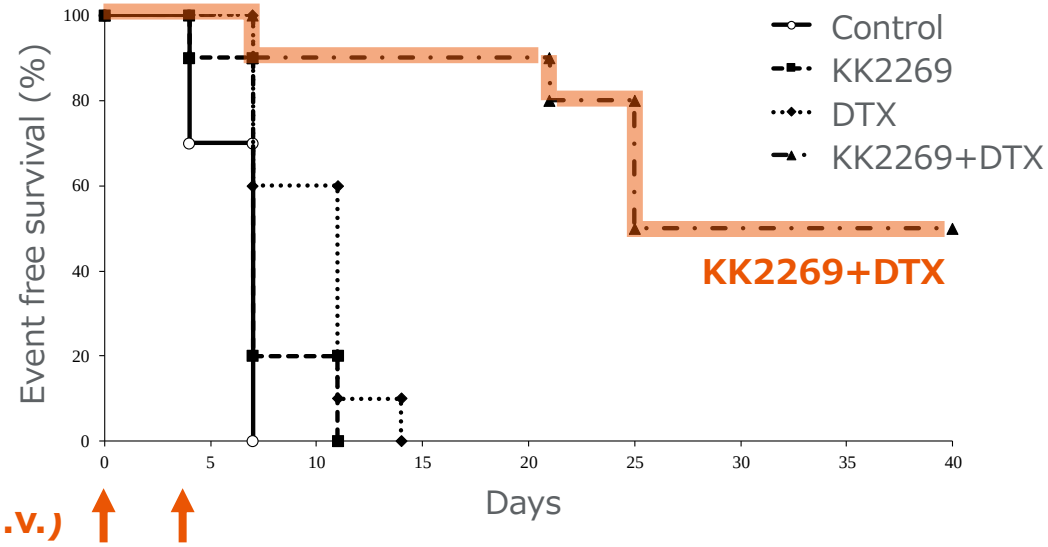
- **KK2269**
- **Control Ig**
- **MEGA CD40L**

*moDC: Monocyte derived DC

KK2269: Efficacy and safety confirmed in non-clinical studies

Survival rate

- Human CD40-expressing Tg mice
- PD1-resistant tumor model
- DTX: Docetaxel



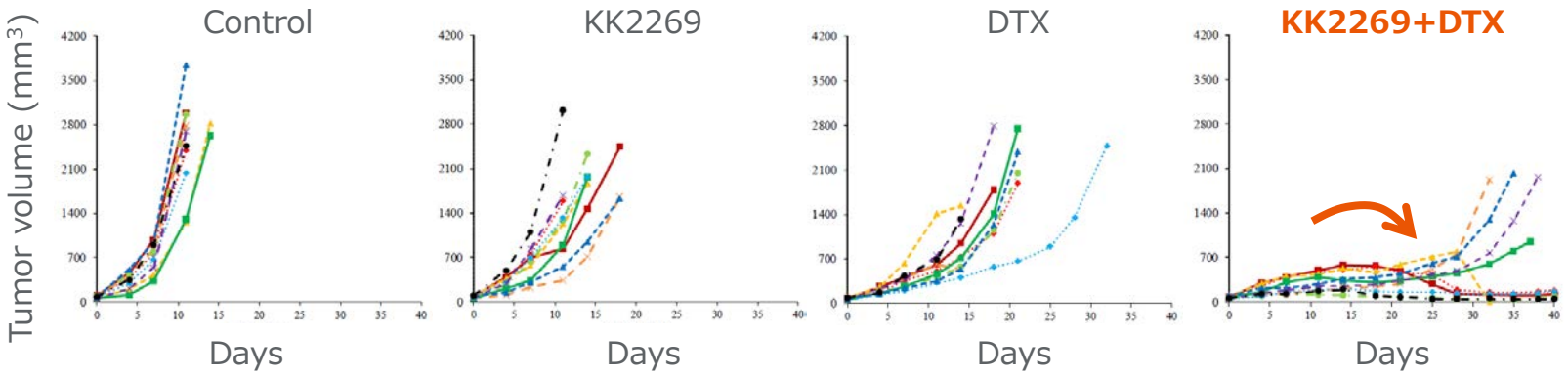
Efficacy

- KK2269 showed remarkable synergy with certain chemotherapy
- Characteristic delayed tumor regression suggesting the induction of de novo anti-tumor immunity (see below).

Safety

- High safety profile observed in cynomolgus monkeys up to 200 mg/kg (the highest dose in the GLP study)

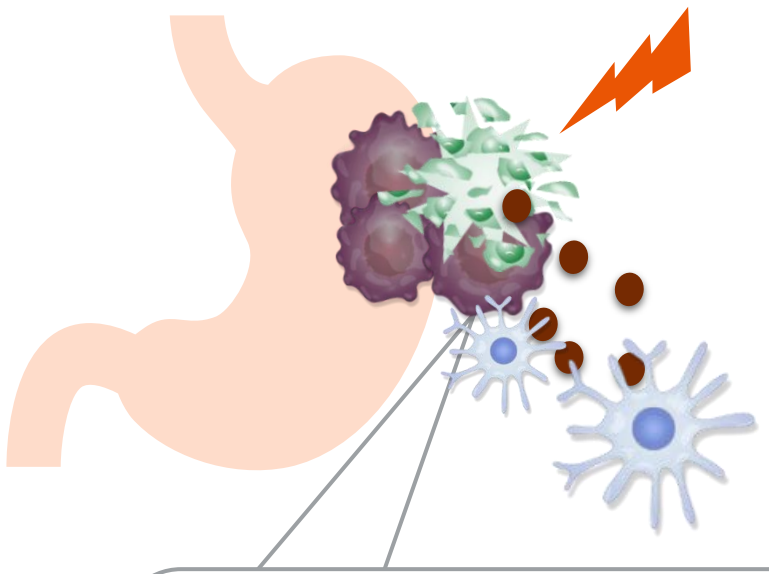
Tumor volume by individual



Non-clinical studies demonstrated the concept: anti-tumor efficacy with high safety

At euthanasia due to criteria or at the study endpoint

Full value of KK2269 in chemo combination



1. Chemo

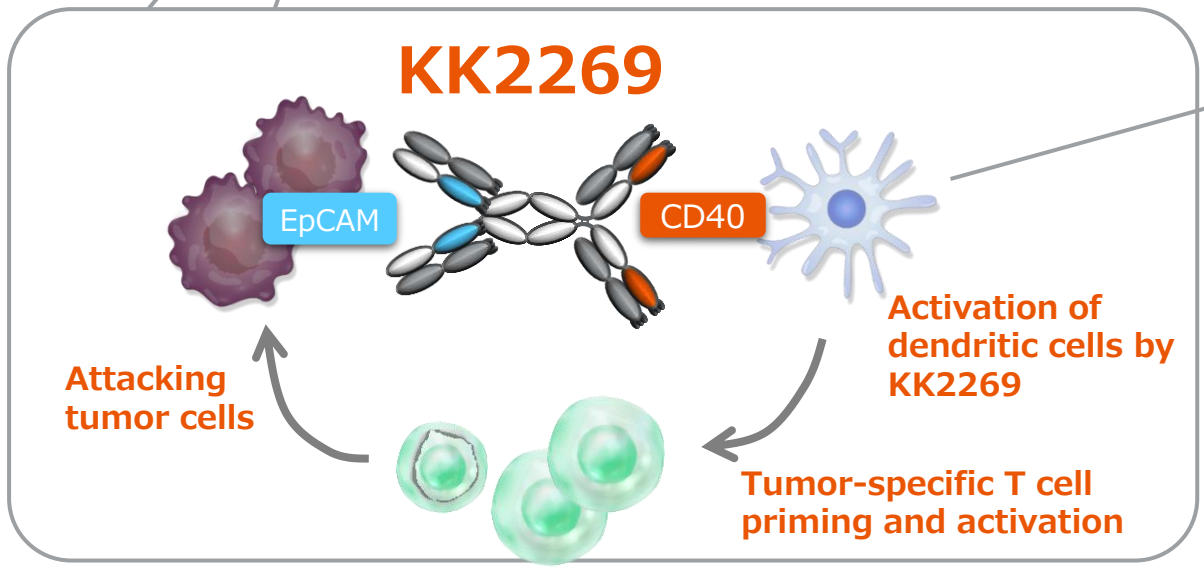
2. Tumor disruption（ICD*）

- Release of tumor antigens and immunostimulants

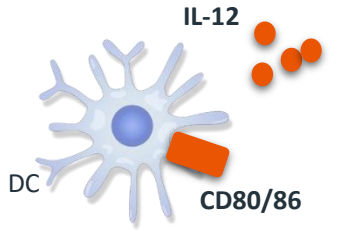
3. Accumulation of dendritic cells in tumors

- Activation
- Tumor antigen uptake

4. Acceleration of the action of KK2269 (tumor-dendritic cell cross-linking)

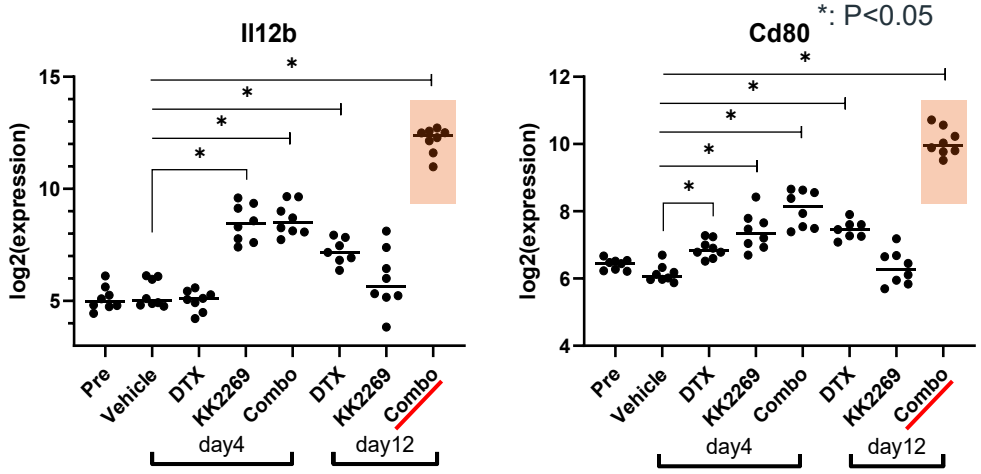


Evaluation of activation of dendritic cells in tumor



cross presentation
Th1/CTL activation

Vital co-stimulatory factors for T cell priming



Synergy of Chemo+KK2269 was confirmed. POC to be obtained in clinical trials

*: Immunogenic cell death

Toward the Successful Creation and Delivery of Life-changing Value

- **KHK4951 (Ph1 study results and Ph2 studies overview)**
- HSC-GT (Orchard Therapeutics plc)

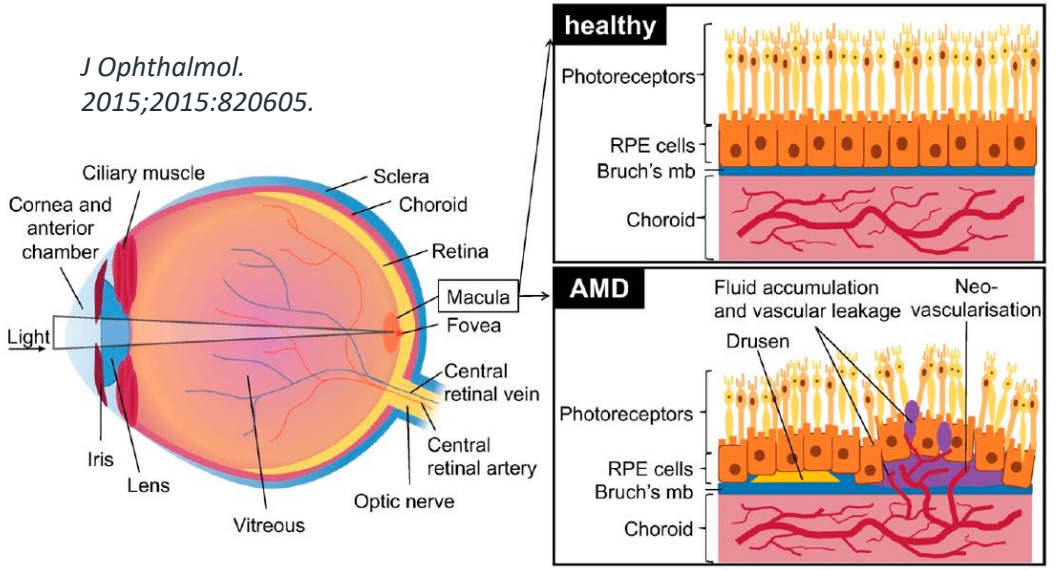
KHK4951: tivozanib eyedrop

- Active ingredient - tivozanib: A small molecule VEGFR inhibitor discovered by Kyowa Kirin with high selectivity and potent activity
- Completed Ph1 study in patients with exudative neovascular age-related macular degeneration (nAMD)

- Abnormal angiogenesis results in macular damage and significant vision impairment
- Caused by VEGF*1 production from retinal pigment epithelial cells
- Drug-treated paitent number
  Japan: approx. 200,000 Global: approx. 1.6 million

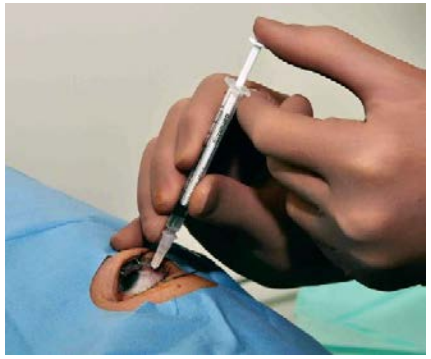
*1: Vascular endothelial Growth Factor

J Ophthalmol. 2015;2015:820605.



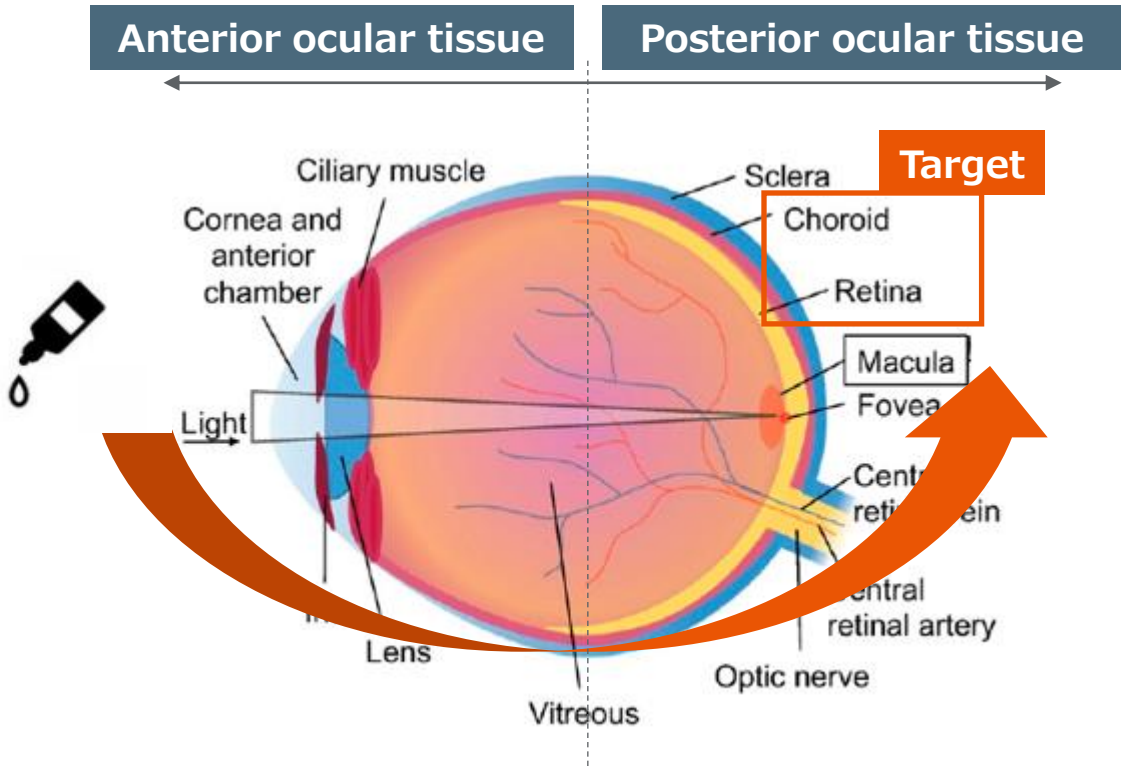
- Standard of Care: Intravitreal injection of anti-VEGF drugs

  Due to invasive administration route and treatment burden (e.g. hospital visit) of the SOC, there is clear medical needs for non-invasive treatment option.



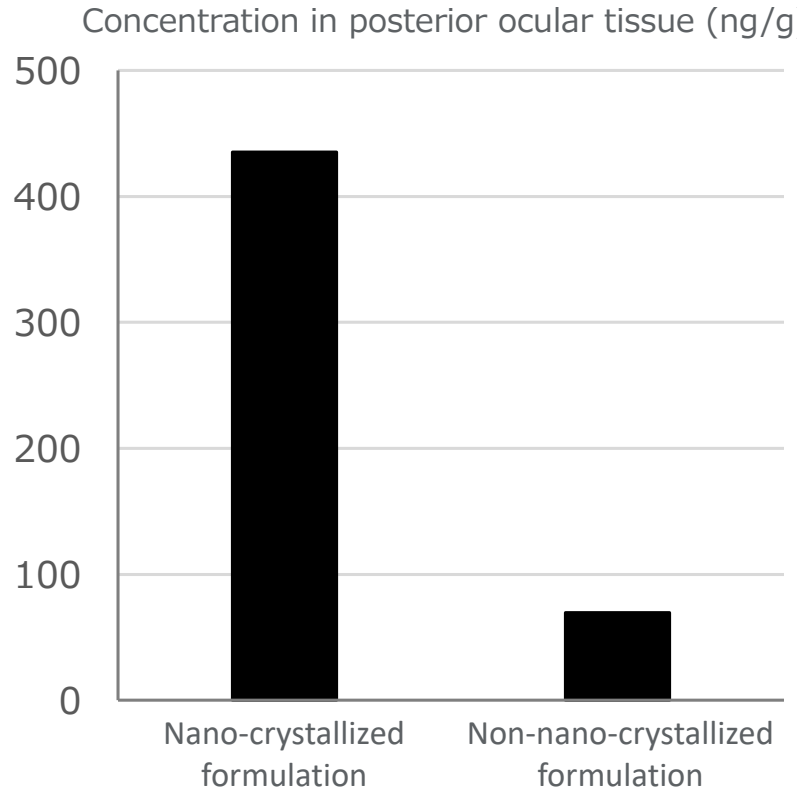
Lancet 2012; 379: 1728–38

Nano-crystallized formulation for delivery of active ingredients to the posterior ocular tissues



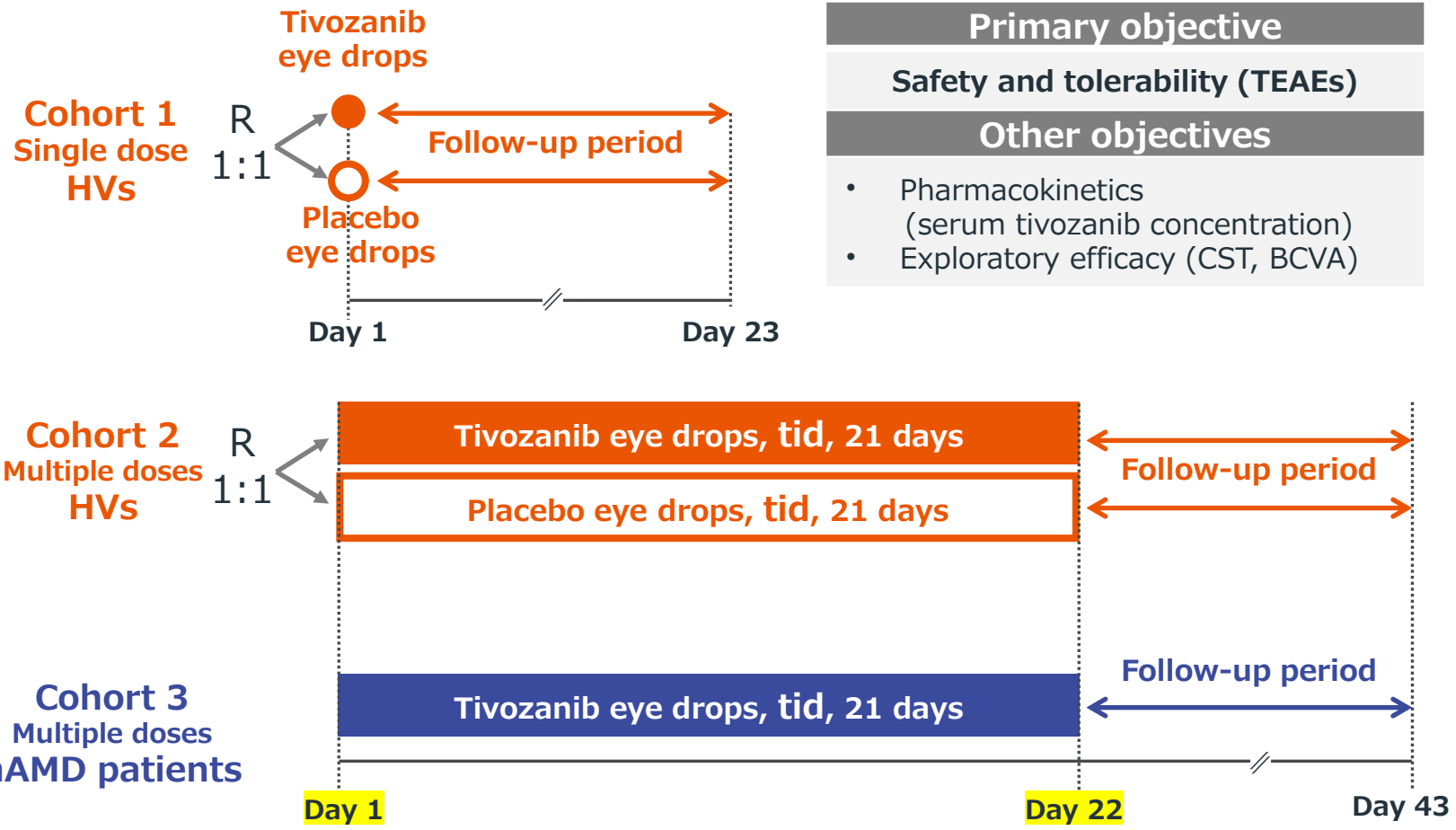
J Ophthalmol. 2015;2015:820605. (partially modified).

Drug concentration in the posterior ocular tissue after topical instillation of tivozanib eye-drop to rats



The nano-crystallized formulation we developed enabled efficient delivery of the active ingredients to the posterior ocular tissues.

Ph1 study



Primary objective

Safety and tolerability (TEAEs)

Other objectives

- Pharmacokinetics (serum tivozanib concentration)
- Exploratory efficacy (CST, BCVA)

Healthy volunteers in cohorts 1 and 2

Inclusion criteria

- Age ≥ 20 to < 50 years
- Visual acuity ≥ 20/20

Exclusion criteria

- Current illness requiring treatment
- Current or history of dry eye

Patients with nAMD* in cohort 3

Inclusion criteria

- **CST ≥ 300 μm**
- **BCVA score ≥ 23 letters**

Exclusion criteria

- Glaucoma, ischemic optic neuropathy, retinitis pigmentosa

* Both treatment-naive and previously anti-VEGF treated patients were enrolled.

BCVA: best corrected visual acuity; CST: central subfield thickness;
HVs: healthy volunteers; R: randomization; TEAE: treatment-emergent adverse event; tid: three times a day.

Ph1 study: Dosage regimen

Single dose

Cohort 1, HVs

- Step 1: 0.5 w/v%, 1 drop Japanese, with NLO
- Step 2: 1.0 w/v%, 1 drop Japanese, with NLO
- Step 3: 1.0 w/v%, 2 drops Japanese, with NLO
- Step 4: 1.0 w/v%, 2 drops White, with NLO
- Step 5: 2.0 w/v%, 1 drop Japanese, with NLO

Multiple doses (tid) for 21 days

Cohort 2, HVs

- Step 1: 0.5 w/v%, 1 drop Japanese, with NLO
- Step 2: 1.0 w/v%, 1 drop Japanese, with NLO
- Step 3: 1.0 w/v%, 2 drops Japanese, with NLO
- Step 4: 1.0 w/v%, 2 drops Japanese, without NLO
- Step 5: 1.0 w/v%, 2 drops White, with NLO
- Step 6: 2.0 w/v%, 1 drop Japanese, with NLO

Cohort 3, nAMD patients

- Step 1: 0.5 w/v%, 1 drop Japanese, with NLO
- Step 2: 1.0 w/v%, 1 drop Japanese, with NLO
- Step 3: 1.0 w/v%, 2 drops Japanese, with NLO

Steps for those without NLO

Steps for white subjects

Steps for 2.0 w/v% formulation

NLO: nasolacrimal duct occlusion or eyelid closure

KYOWA KIRIN

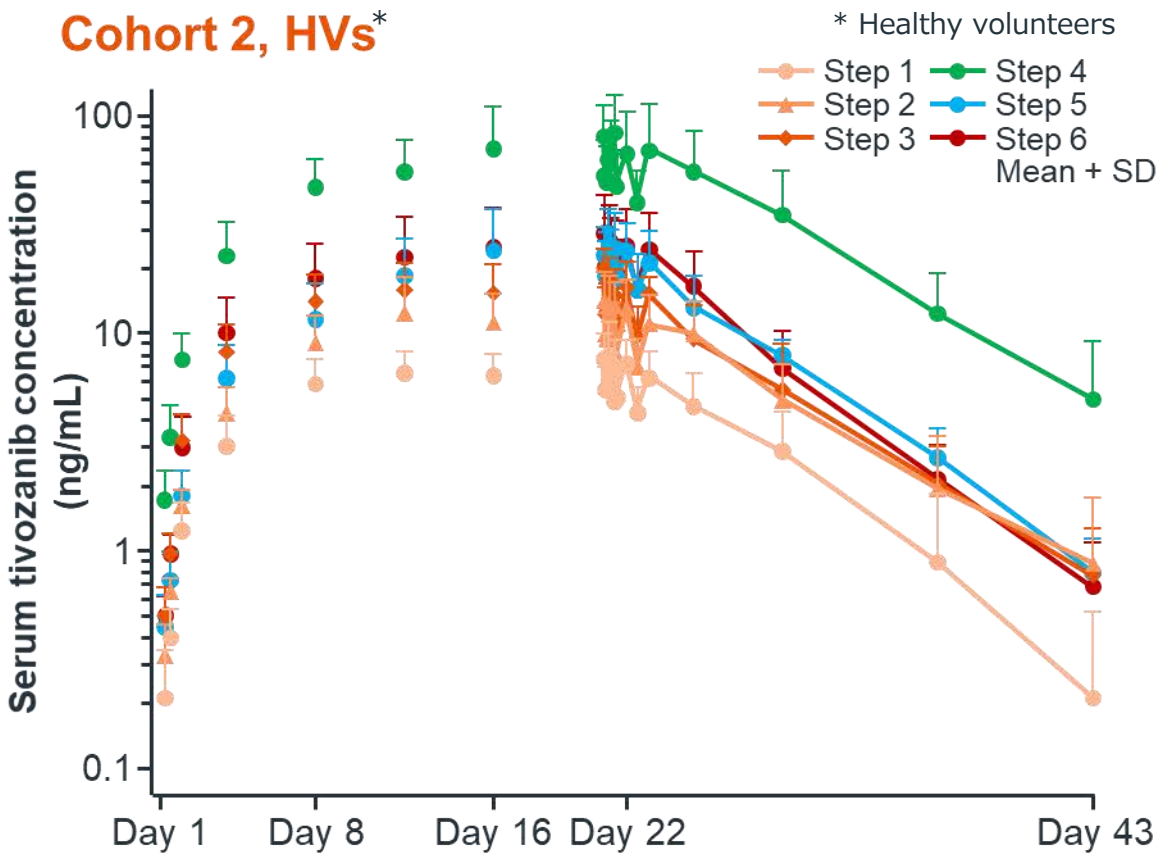
Ph1 study: Safety

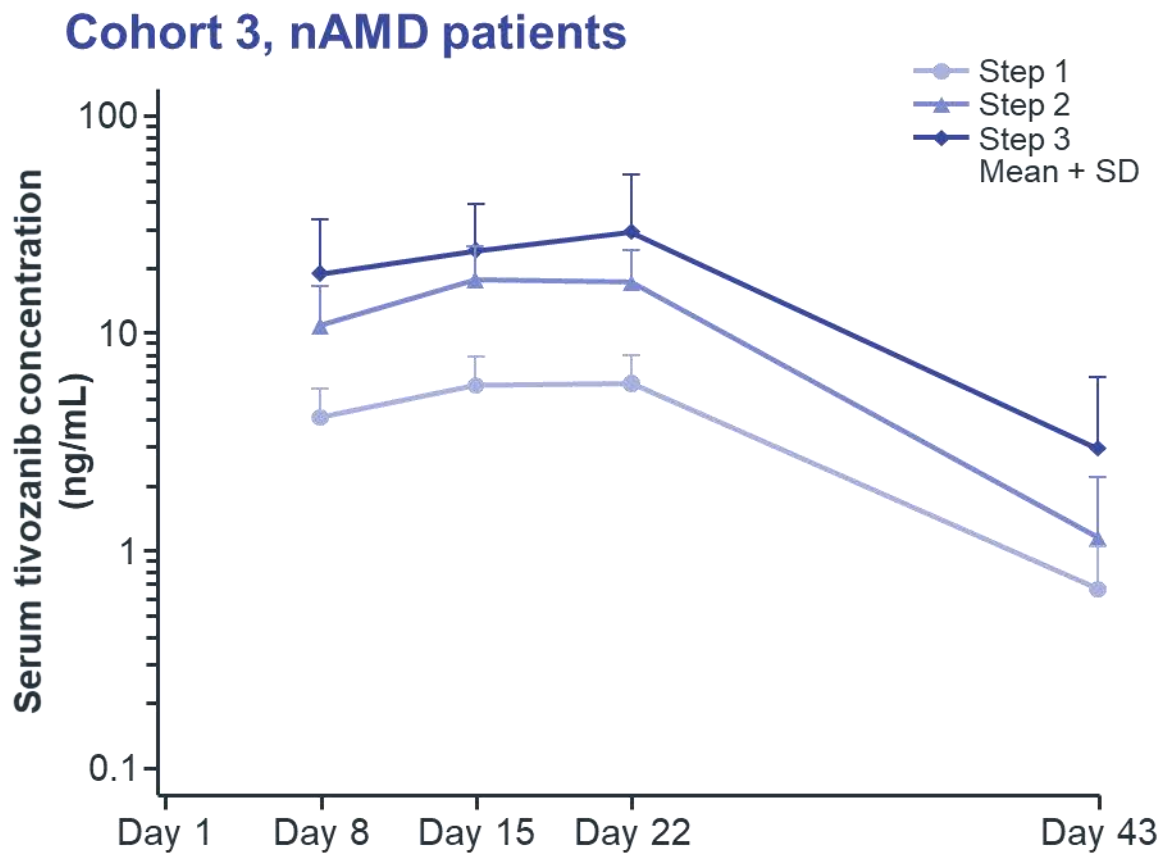
Any TEAE or ocular AE in the study eye	Placebo (tid), HVs (n = 12)		Tivozanib (tid), HVs												Tivozanib (tid), nAMD patients							
			Step 1 Jpn with* 0.5 w/v% 1 drop (n = 6)		Step 2 Jpn with* 1.0 w/v% 1 drop (n = 6)		Step 3 Jpn with* 1.0 w/v% 2 drops (n = 6)		Step 4 Jpn without† 1.0 w/v% 2 drops (n = 6)		Step 5 White with* 1.0 w/v% 2 drops (n = 6)		Step 6 Jpn with* 2.0 w/v% 1 drop (n = 6)		HVs Total (n = 36)		Step 1 Jpn with* 0.5 w/v% 1 drop (n = 7)		Step 2 Jpn with* 1.0 w/v% 1 drop (n = 10)		Step 3 Jpn with* 1.0 w/v% 2 drops (n = 11)		nAMD patients Total (n = 28)	
Any TEAE, n (%)	2	(16.7)	3	(50.0)	4	(66.7)	6	(100.0)	6	(100.0)	4	(66.7)	5	(83.3)	28	(77.8)	3	(42.9)	4	(40.0)	5	(45.5)	12	(42.9)
Death, other serious, or other significant	0		0		0		0		0		0		0		0		0		0		0		0	
Eye disorders, n (%)	1	(8.3)	2	(33.3)	4	(66.7)	2	(33.3)	6	(100.0)	3	(50.0)	5	(83.3)	22	(61.1)	1	(14.3)	4	(40.0)	3	(27.3)	8	(28.6)
Punctate keratitis	1	(8.3)	2	(33.3)	2	(33.3)	1	(16.7)	6	(100.0)	3	(50.0)	3	(50.0)	17	(47.2)	0		1	(10.0)	3	(27.3)	4	(14.3)
Eye irritation	0		0		3	(50.0)	1	(16.7)	4	(66.7)	1	(16.7)	3	(50.0)	12	(33.3)	0		2	(20.0)	0		2	(7.1)
Foreign body sensation in eyes	0		0		0		0		1	(16.7)	0		1	(16.7)	2	(5.6)	0		0		0		0	
Vision blurred	0		0		0		0		1	(16.7)	0		0		1	(2.8)	0		0		0		0	
Eye pruritus	0		0		0		0		0		1	(16.7)	0		1	(2.8)	0		0		0		0	
Eye pain	0		0		0		0		0		0		0		0		0		1	(10.0)	0		1	(3.6)
Lacrimation increased	0		0		0		0		0		0		0		0		0		1	(10.0)	0		1	(3.6)
Pinguecula	0		0		0		0		0		0		0		0		1	(14.3)	0		0		1	(3.6)
Swelling of eyelid	0		0		0		0		0		0		0		0		0		1	(10.0)	0		1	(3.6)

TEAE: any adverse event (AE) that occurred or worsened in the period between the first administration of the study drug and the end of the study; death: any AE with an outcome of 'fatal'; other serious: serious AEs other than death; other significant: non-serious AEs leading to withdrawal of the investigational product. *With nasolacrimal duct occlusion or eyelid closure. † Without nasolacrimal duct occlusion or eyelid closure. Jpn: Japanese.

No serious adverse events leading to study discontinuation were observed in either HVs or Japanese nAMD patients

Ph1 study: Serum Drug Concentration





- Mean serum concentrations of tivozanib increased in a dose-dependent manner.
- No significant differences in serum pharmacokinetics were observed between HVs and nAMD patients.

KHK4951 Ph1 study summary

Safety	• There were **no serious AEs or AEs leading to discontinuation**. • **There were no remarkable differences in its safety profiles between Japanese and White, and between HVs and nAMD patients.**
Pharmaco-kinetics	• Mean serum tivozanib concentration increased in a dose-dependent manner. • No significant differences in serum concentration were found between HVs and nAMD patients.

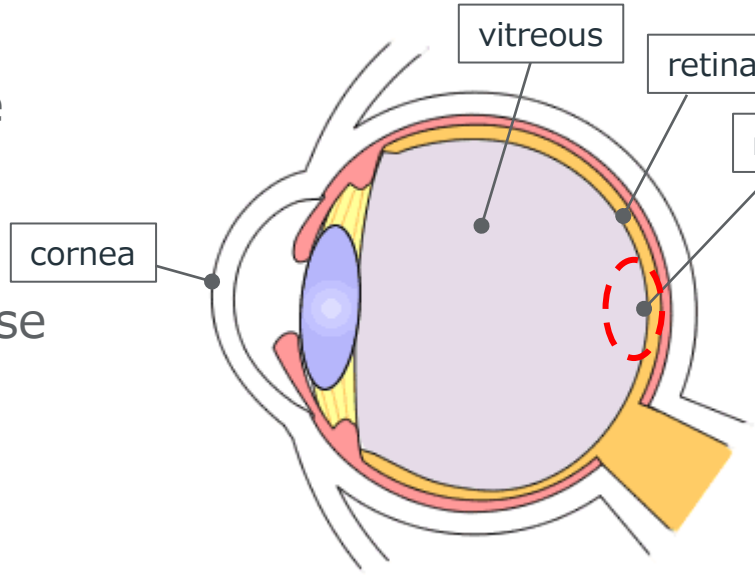
+ Exploratory evaluation of efficacy also conducted

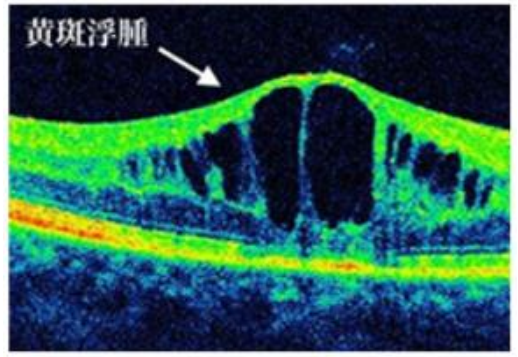
Decided to conduct Ph2 study based on the Ph1 study results

Diabetic Macular Edema (DME)

*Target indication for Ph2 study

- As a complication of diabetic retinopathy, high blood sugar causes damage to capillaries in the macula, resulting in edema of the macula and impairment of vision
- VEGF contributes the development of the disease
- Number of patients treated with drugs:
  - Japan: approx. 140K, Global: approx. 1.3M
- Standard of Care:
  - Intravitreal injection of anti-VEGF drugs or steroids, or intraocular implants
  - Ocular surgery (vitrectomy, laser treatment)





References : https://www.civillink.net/fsozai/eye.html
https://www.eye.med.kyushu-u.ac.jp/patient/question/index3.html

Current treatment methods are all highly invasive
A need for less invasive treatment options

KHK4951 Ph2 study overview

Locations	• (For both studies) JP, US, AU, KR
Study Completion (estimated)	• (For both studies) 2026Q1
Enrollment (estimated)	• nAMD 180, DME 150
Primary Endpoint	• Reduction of 15 or more letters in BCVA (Best corrected visual acuity) as measured by ETDRS[2] visual acuity chart from baseline

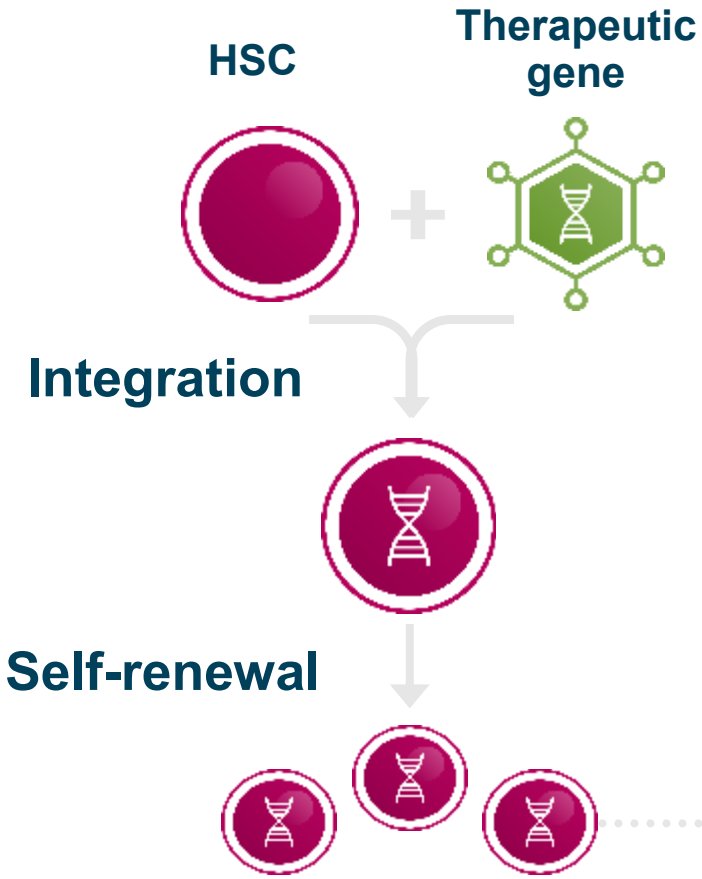
Participant Group/Arm	Intervention/Treatment
Experimental: Arm A KHK4951 High dose	• Drug: KHK4951 KHK4951 eye drop for 44(nAMD)/36(DME) weeks until end of the trial • Drug: Aflibercept Injection Intravitreal injection (IVT) of aflibercept will be given as specified in the protocol
Experimental: Arm B KHK4951 Middle dose	
Experimental: Arm C KHK4951 Low dose	

1. Clinical Trials.gov ID: NCT06116890 (nAMD), NCT06116916 (DME); jRCT ID: jRCT2031230401 (nAMD), jRCT2031230400 (DME) 2. Early Treatment Diabetic Retinopathy Study

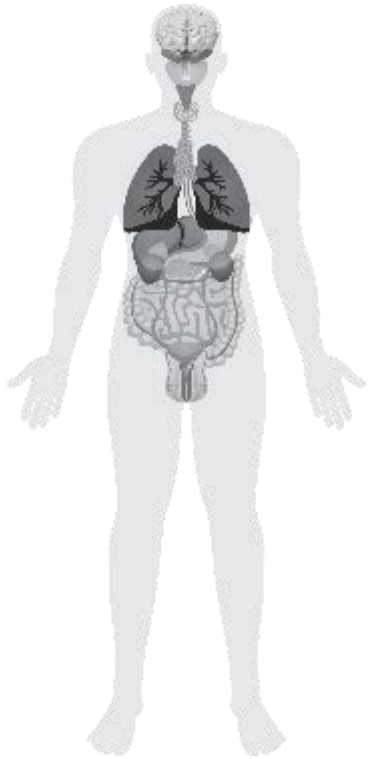
Toward the Successful Creation and Delivery of Life-changing Value

- KHK4951 (Ph1 study results and Ph2 studies overview)
- **HSC-GT (Orchard Therapeutics plc)**

Hematopoietic Stem Cell Gene Therapy (HSC-GT)



- Monocyte / Macrophage
- Granulocyte
- T cells
- B cells
- NK cells
- Megakaryocyte
- Erythrocyte



- Brain
- GI

High area of focus

- Other Organ Systems

Areas for potential future expansion

HSC-GT allows delivery of gene-modified blood/immune cells to any part of the body

Literature references: Alessia Capotondo, Rita Milazzo, Letterio Salvatore Politi, Angelo Quattrini, Alessio Palini, Tiziana Plati, Stefania Merella, Alessandro Nonis, Clelia di Serio, Eugenio Montini, Luigi Naldini, and Alessandra Biffi, PNAS September 11, 2012 109 (37) 15018-15023; https://doi.org/10.1073/pnas.1205858109; Tissue macrophages: heterogeneity and functions, Siamon Gordon and Annette Plüddemann, BMC Biology 2017 15:53, 29 June 2017

Gene Therapy Manufacturing

GMP Cell Product Manufacturing Platform

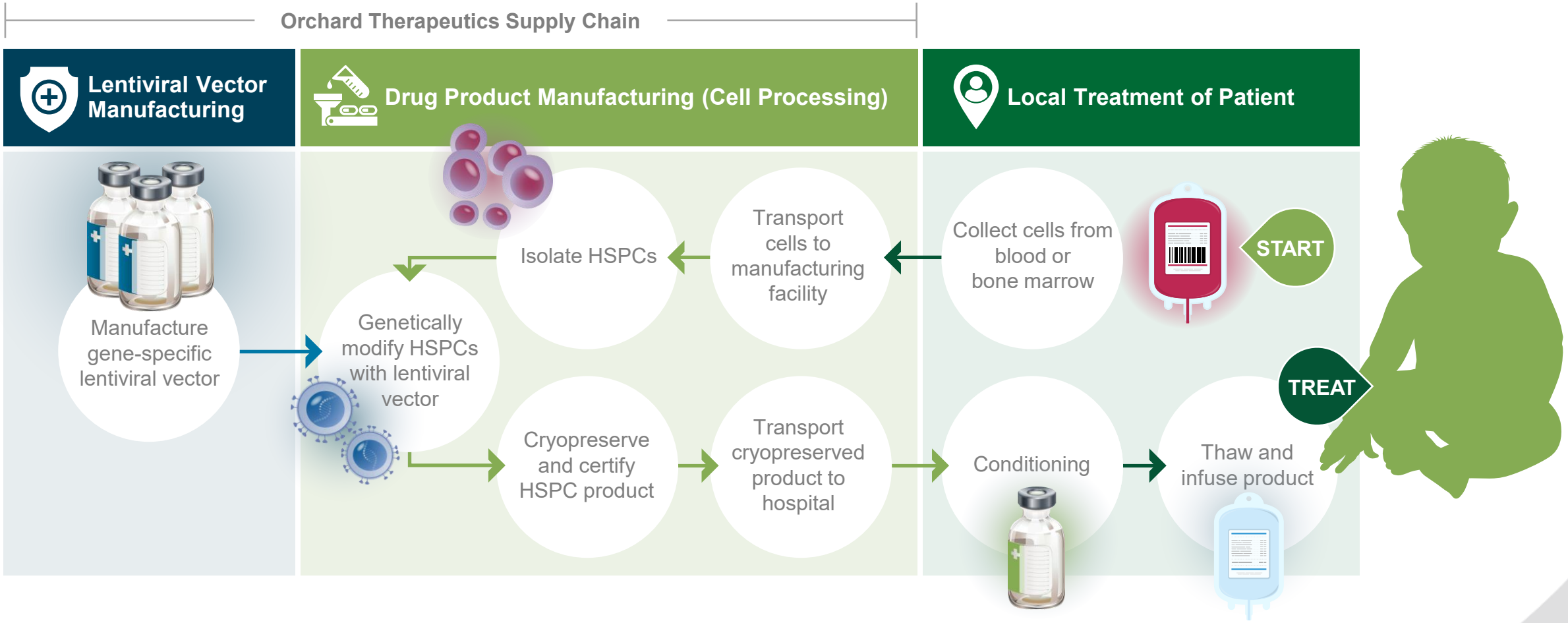


Figure: Created by Orchard Therapeutics plc

Delivering Proteins to Brain

Potential to Treat Multi-System Neurometabolic Diseases via Cross-Correction

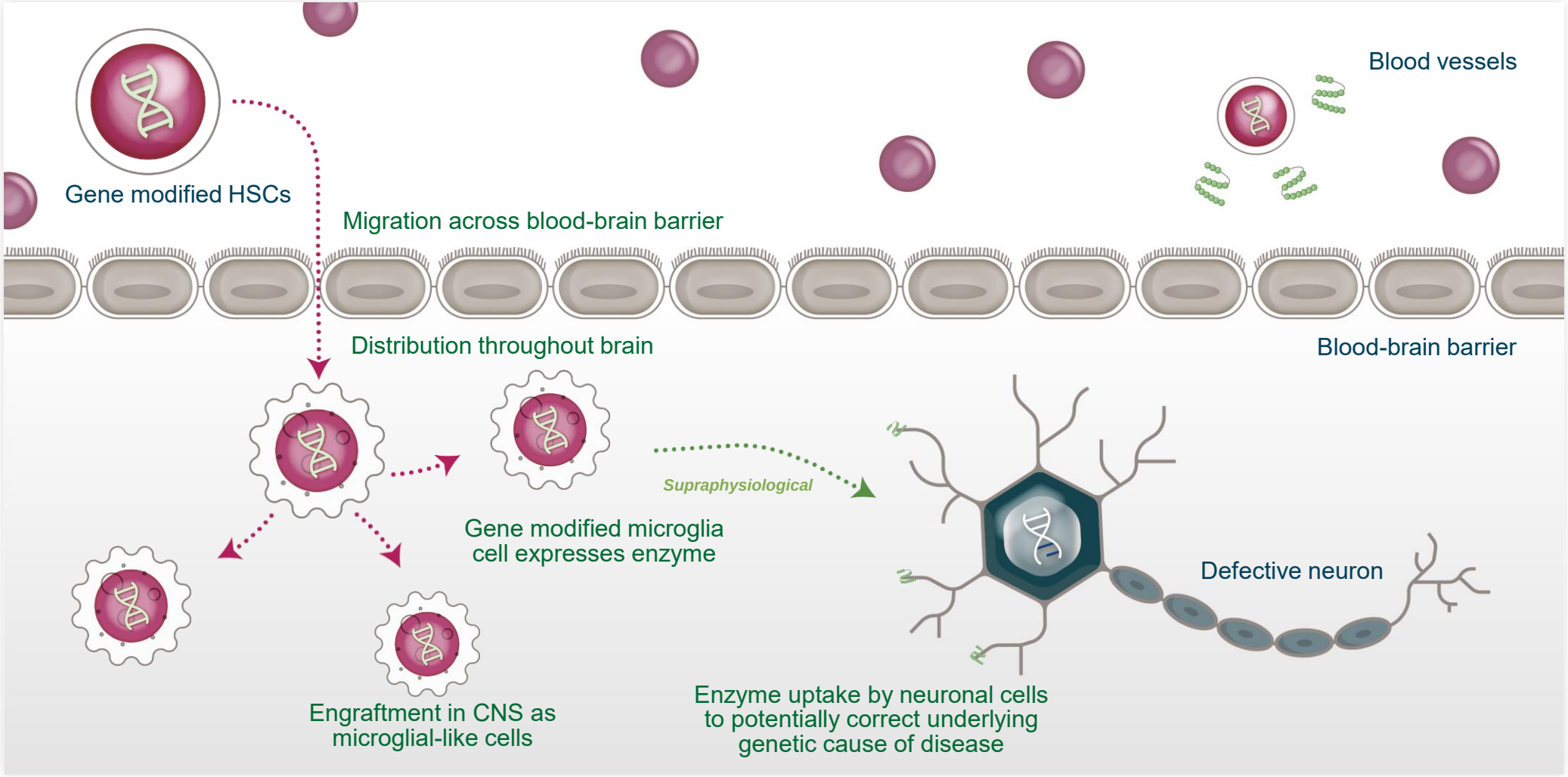


Figure: Created by Orchard Therapeutics plc

Libmeldy® (OTL-200, atidarsagene autotemcel)

- MLD (Metachromatic Leukodystrophy)
  - Fatal genetic CNS disorder
  - Rapid and irreversible loss of motor and cognitive function
  - In its most severe form, most children pass away within five years of symptom onset[1]

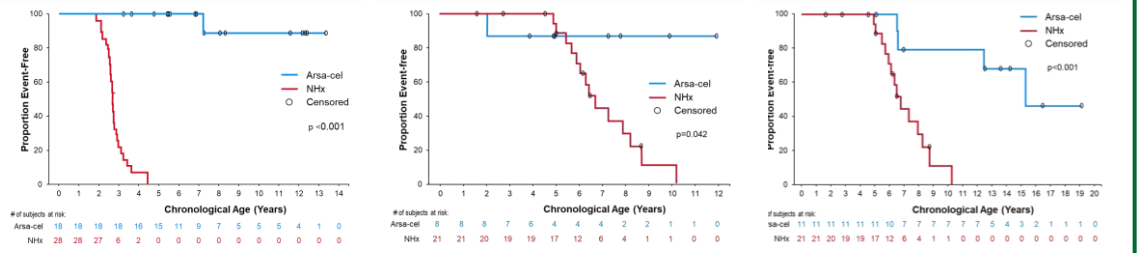
Status	Next Catalyst	Expected timing of Catalyst
Launched in Europe Filed in US	FDA approval	PDUFA: March 18, 2024

Severe Motor Impairment Free Survival (sMFS)

Interval from birth to first occurrence GMFC-MLD ≥ 5 (no locomotion and unable to sit) or death

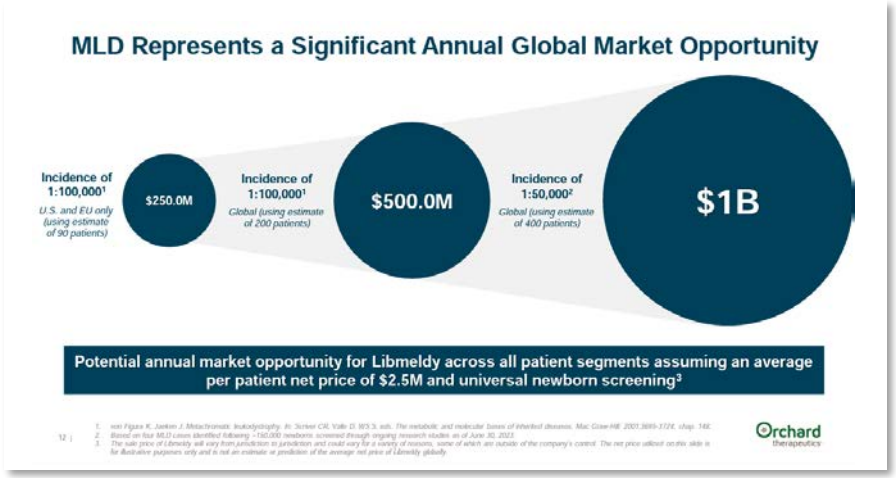
Treatment with OTL-200 resulted in statistically significant and clinically meaningful improvement in sMFS in the PSLI (p<0.001), PSEJ (p=0.042) and ESEJ (p<0.001) MLD subgroups compared to disease natural history.

	Pre-Symptomatic Late Infantile (PSLI)	Pre-Symptomatic Early Juvenile (PSEJ)	Early-Symptomatic Early Juvenile (ESEJ)
OTL-200	100%	87.5%	80%
NHx	0%	11.2%	11.2%



Data presented at the at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium 2023, August 2023

Ref.) Orchard Therapeutics plc, Q2 2023 Financial Results and Webcast https://ir.orchard-tx.com/static-files/9fed8b65-2fd9-491a-97c0-69bf6595c0c3



Potential annual market opportunity for Libmeldy® across all patient segments assuming an average per patient net price of $2.5M and universal newborn screening[2]

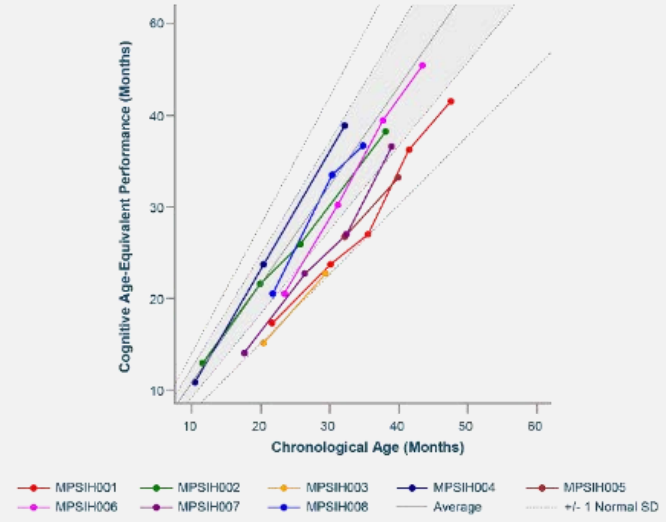
1. van Rappard DF, Boelens JJ, Wolf NI. Metachromatic leukodystrophy: disease spectrum and approaches for treatment. Best Pract Res Clin Endocrinol Metab 2015; 29: 261–73.
2. The sale price of Libmeldy® will vary from jurisdiction to jurisdiction and could vary for a variety of reasons, some of which are outside of the company's control. The net price utilized on this slide is for illustrative purposes only and is not an estimate or prediction of the average net price of Libmeldy® globally.

Development Pipelines: OTL-203, OTL-201

OTL-203

- Indication: MPS-IH[1]
  - Multisystemic neurometabolic condition affecting cognition, growth and skeletal function
  - ~1:100,000 live births; NBS[2] established in some geographies, incl. U.S.
- Current Status
  - Interim PoC results published in NEJM[3]
  - Moving into a Pivotal (Ph3) study in 2H 2023

Neuropsychological Tests over Time
Cognitive Age-Equivalent Score (Overall)

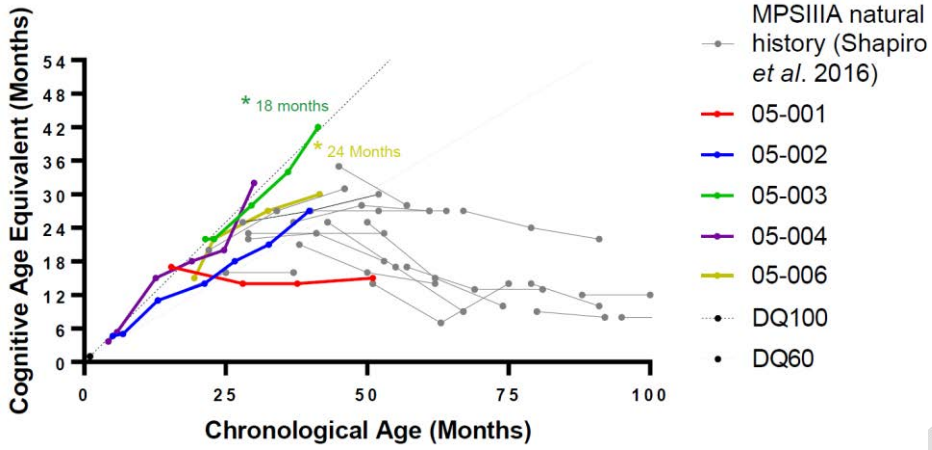


Interim Proof-of-Concept (PoC) Study Results Published in *NEJM*

OTL-201

- Indication: MPS-IIIA [4]
  - Accumulation of substrate heparan sulfate leading to severe CNS degeneration w/ somatic manifestations
  - Development slows from 3 years of age, followed by cognitive decline, behavioral disturbances, loss of skills and eventual death, No successful treatment options
- Current Status
  - PoC study (Ph1/2) is ongoing
  - Biochemical/clinical data reported in 2023 ASGCT meeting

Developmental Age Equivalent[2]



1. Mucopolysaccharidosis type I, Hurler syndrome; 2. Newborn Screening; 3. Engl J Med 2021; 385:1929-1940 DOI: 10.1056/NEJMoa2106596; 4. Mucopolysaccharidosis type IIIA (Sanfilippo Syndrome type A)

Expected Synergy

Further Development as a Japan-Based Global Specialty Pharmaceutical Company

- To be a Japan-based Global Specialty Pharmaceutical Company providing life-changing value to high unmet medical needs in concert with our existing business through Crysvita and Poteligeo

Reinforcement of Innovative New Drug Discovery & Development

Kyowa Kirin

- Experience and expertise of R&D and commercialization in Biologics and Antibody Drugs
- Proprietary next-generation antibody technology
- Continuous efforts on new modalities

×

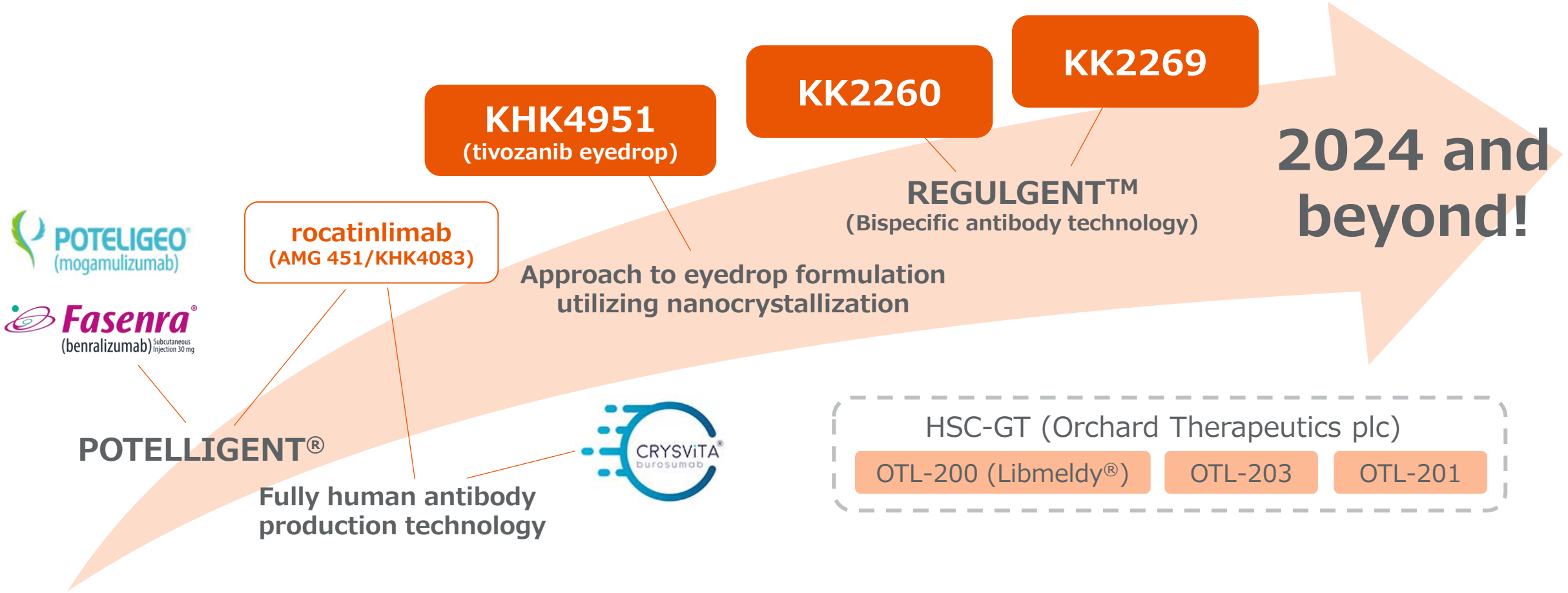
Orchard Therapeutics

- Experience and know-how in the marketing HSC-GT[1] in EU
- High technology in HSC-GT[1] (Research, CMC, SCM, etc.)
- Patient access and collaboration with medical institutions
- Efforts and experience in new modalities

1. Hematopoietic Stem Cell Gene Therapy

- A key step toward delivering advanced value to patients
  - Pursuing the potential for “One-time treatment in life”
  - Challenge to correct the underlying cause of a genetic disease
  - Personalized medicine / Precision medicine
  - Providing treatment beyond the existing drugs
- Address a broader range of UMNs

Innovative New Drug Creation by Kyowa Kirin Drug Discovery Technology



Kyowa Kirin will realize the successful creation and delivery of life-changing value that ultimately makes people smile


Kyowa KIRIN