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Rationale and Design of VOYAGER: Long-term Outcomes of Faricimab and Port Delivery System with Ranibizumab for Neovascular Age-Related Macular Degeneration and Diabetic Macular Edema in Clinical Practice

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Purpose: To describe the rationale and design of the VOYAGER (NCT05476926) study, which aims to investigate the safety and effectiveness of faricimab and the Port Delivery System with ranibizumab (PDS) for neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) in clinical practice. VOYAGER also aims to understand drivers of clinical practice treatment outcomes by gaining novel insight into the intersection of treatment regimens, decisions, anatomic outcomes, and vision.

Design: Primary data collection, noninterventional, prospective, multinational, multicenter clinical practice study.

Participants: At least 5000 patients initiating/continuing faricimab or PDS for nAMD/DME (500 sites, 31 countries).

Methods: Management will be per usual care, with no mandated scheduled visits/imaging protocol requirements. Using robust methodologies, relevant clinical and ophthalmic data, including visual acuity (VA), and data on treatment clinical setting/regimens/philosophies, presence of anatomic features, and safety events will be collected. Routinely collected fundus images will be uploaded to the proprietary Imaging Platform for analysis. An innovative investigator interface will graphically display the patient treatment journey with the aim of optimizing treatment decisions.

Main Outcome Measures: Primary end point: VA change from baseline at 12 months per study cohort (faricimab in nAMD and in DME, PDS in nAMD). Secondary end points: VA change over time and per treatment regimens (fixed, treat-and-extend, pro re nata, and other) and number. Exploratory end points: VA change in relation to presence/location of anatomic features that impact vision (fluid, central subfield thickness, fibrosis, atrophy, subretinal hyperreflective material, diabetic retinopathy severity, and disorganization of retinal inner layers) and per treatment regimen/philosophies. The impact of regional and practice differences on outcomes will be assessed as will safety.

Results: Recruitment commenced in November 2022 and will continue until late 2027, allowing for up to 5 years follow-up. Exploratory interim analyses are planned annually.

Conclusions: VOYAGER is an innovative study of retinal diseases that will assess the effectiveness and safety of faricimab and PDS in nAMD and DME and identify clinician- and disease-related factors driving treatment outcomes in clinical practices globally to help optimize vision outcomes.

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Anti-VEGF-A agents have transformed vision outcomes for the increasingly prevalent retinal vascular diseases, diabetic macular edema (DME) and neovascular age-related macular degeneration (nAMD).[1–4] However, vision outcomes in clinical practice studies often fall short of those in clinical trials[5–7] and are often not maintained long-term.[8–10] In clinical practice studies, loss of 5.2 letters[8] and cumulative incidence of sight impairment and legal blindness of 53.7% and 15.6%,[11] respectively, have been shown at 4 years in patients receiving anti-VEGFs for nAMD.

Multiple factors may contribute to poorer outcomes in clinical practice,[12] with inadequate treatment frequency often suggested as the main factor.[13] However, other factors may also underlie the poorer outcomes. Diversity in clinical presentation and social determinants of health may result in clinical practice patient populations responding differently to treatment when compared with clinical trial populations.[12] Furthemore, the inability to replicate the complex treatment algorithms and imaging protocols of trials, along with inadvertent delays to treatment initiation or lapses in treatment in clinical practice, more common among patients of lower socioeconomic status, may result in differences in treatment outcomes.[14–18] Because clinical trials often have shorter follow-up than clinical practice studies,[19,20] there is also a lack of evidence to inform strategies for long-term treatment when other causes of vision loss, such as atrophy and fibrosis, are more common.[15] Additionally, variations in eye examination and imaging interpretation, treatment philosophies, outcome goals, regional disease and management guidelines, and clinical training likely result in heterogenous disease management.[21–23] These factors need to be assessed to implement appropriate strategies that can help close the gap between clinical practice and clinicial trial outcomes.

Data collection and reporting in existing clinical practice registries throughout the globe has generally been limited, often to visual acuity (VA) outcomes, interventions used, and numbers of intravitreal injections received.[24–26] Although these studies report what is happening in clinical practice, they do not examine other key drivers impacting vision outcomes or the reasons driving treatment decisions. Furthermore, in clinical practice studies to date, there has been limited access to routinely taken images and, therefore, there has been no way to determine or validate the impact of factors, such as clinican disease activity interpretation and key anatomic determinants of vison loss on outcomes.

Two novel products have recently become available for retinal indications: faricimab, a bispecific antibody that provides dual anti-VEGF-A and angiopoietin-2 inhibition, and the Port Delivery System with ranibizumab (PDS), a permanent refillable ocular implant that provides up to 6 months of uninterrupted ranibizumab therapy (Lim JI, Wells JA, Eichenbaum DA, et al. Efficacy, durability, and safety of faricimab in diabetic macular edema: 2-year results from the phase 3 YOSEMITE and RHINE trials. Paper presented at the Association for Research in Vision and Ophthalmology; May 1−5, 2022; Denver, CO).[19,27–29] Both offer the possibility for increased treatment durability without compromising visual outcomes, thereby potentially reducing the treatment burden for patients compared with current standards of care. A deeper understanding of the many factors that affect outcomes, including anatomic factors and treatment regimens/decisions/philosophies that have been inadequately addressed in previous clinical practice studies, and shortcomings in current disease management may be key to optimizing outcomes with these newly approved medications.

Here, we describe the rationale and methodology of the VOYAGER study (NCT05476926), which aims to investigate the long-term effectiveness and safety of faricimab and PDS for nAMD and DME in routine clinical practice. VOYAGER is unique because it will provide comprehensive information on the drivers of clinical practice treatment outcomes by assessing and evaluating the relationships between treatment regimens and philosophies, treatment decisions, anatomic features, and vision as well as the ability to verify key features on the images provided. As such, VOYAGER will provide novel information that will help explain the differences in treatment outcomes between clinical practice and clinical trials and therefore help to optimize the global treatment outcomes for these retinal diseases.

Methods

Study Design

VOYAGER is a long-term, primary data collection, noninterventional, prospective, multinational, multicenter study of faricimab and PDS in nAMD and DME (study cohorts: faricimab in nAMD, faricimab in DME, and PDS in nAMD) in routine clinical practice. Additional in-scope products and indications will be allowed once approval has been obtained from regulatory authorities.

Patient enrollment will be initiated after approval by institutional review boards/ethics committees. The study will be conducted in accordance with the Guidelines for Good Publication Practice and local laws and regulations as applicable. Written informed consent will be obtained before any data are collected.

At least 5000 patients over 500 sites globally with commercial availability/reimbursement and access to faricimab or PDS are planned to be enrolled in VOYAGER (Fig 1). Selected sites, including rural/remote sites, will encompass a variety of clinical practice settings (public/private) and clinician experience (years of practice and prior trial participation).

Once enrolled, disease management will be at the treating clinicians' discretion in accordance with local practice and labeling. There will be no scheduled clinic visits or required imaging protocols. Patients will be followed up from enrollment until study end, death, withdrawal of consent, interventional ophthalmology clinical trial participation, early study termination, or study site discontinuation.

VOYAGER will be conducted from November 2022 until the end of 2027, allowing for up to 5 years of follow-up (Fig 2).

Steering Committee and Patient Partnership Group

The VOYAGER Steering Committee comprises ophthalmologists with retinal subspeciality training who provide scientific and medical expertise on the study design, protocol development, the Statistical Analysis Plan, and study implementation and will review any relevant study-related documents or procedures to ensure timely and complete collection of accurate study data. The Patient

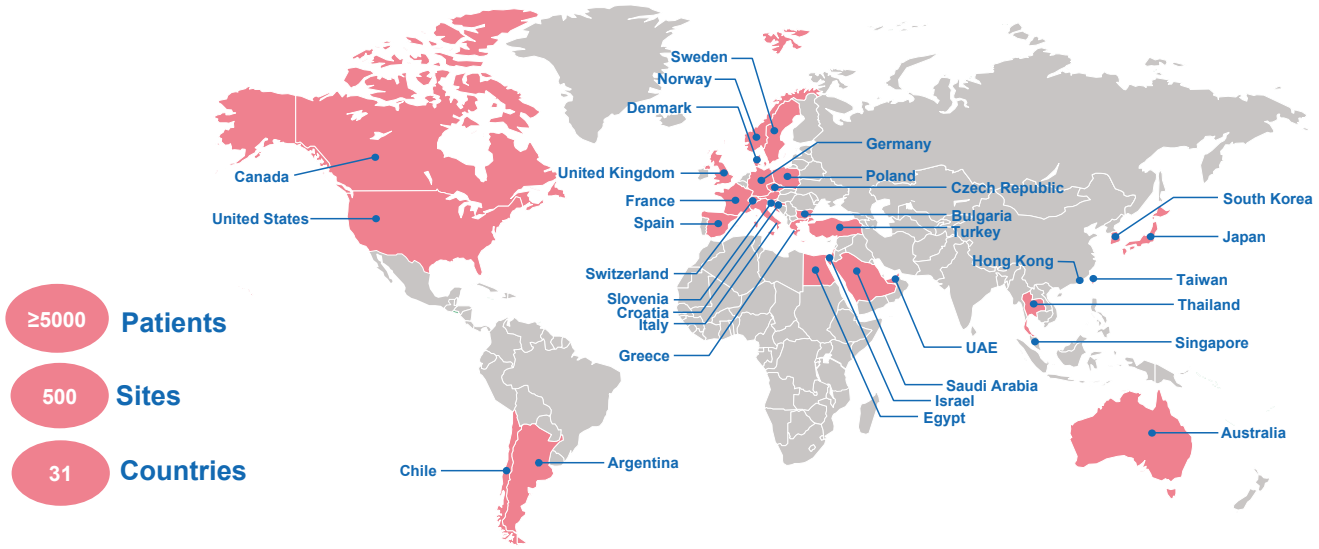

Figure 1. Countries with sites participating in the VOYAGER study. UAE = United Arab Emirates.

Partnership Group has also reviewed the informed consent form and patient- and site-facing materials to ensure relevance to stakeholders.

Eligibility Criteria

Inclusion criteria are broad to reflect clinical practice. Patients will be eligible for study entry if they are adult patients (defined by local regulations and product labels), provide signed informed consent, and are currently being treated or will be initiating treatment with faricimab or PDS for an approved retinal indication (currently nAMD or DME). Patients from Roche interventional studies continuing faricimab or PDS will also be eligible, and there is no limit on the number of patients who can roll over from a Roche interventional trial. Patients currently using, or who have previously used, other anti-VEGFs are eligible if they will be switching to faricimab or PDS. Patients will continue in the study if they stop treatment or switch to another treatment during the study.

The only exclusion criterion is participation in another ophthalmology clinical trial involving treatment with any investigational drug or procedure within 28 days before enrollment.

Objectives and End Points

The primary objective is to evaluate the clinical practice effectiveness of faricimab and PDS. The primary end point will assess VA change (approximate ETDRS letter score) from baseline at 12 months (nearest visit to 12 months). A key secondary end point will assess VA change over designated timepoints (nearest visits to 3, 6, 24 months, and annually thereafter). Other key secondary end points will evaluate correlation of retinal treatment regimens (pro re nata, fixed, treat-and-extend, and other) and number of treatments/visits with VA change over time.

Exploratory end points will evaluate the impact of presence and location of fluid, central subfield thickness reduction, and specific anatomic features (fibrosis, atrophy, subretinal hyperreflective material, hyperreflective foci, diabetic retinopathy severity, and

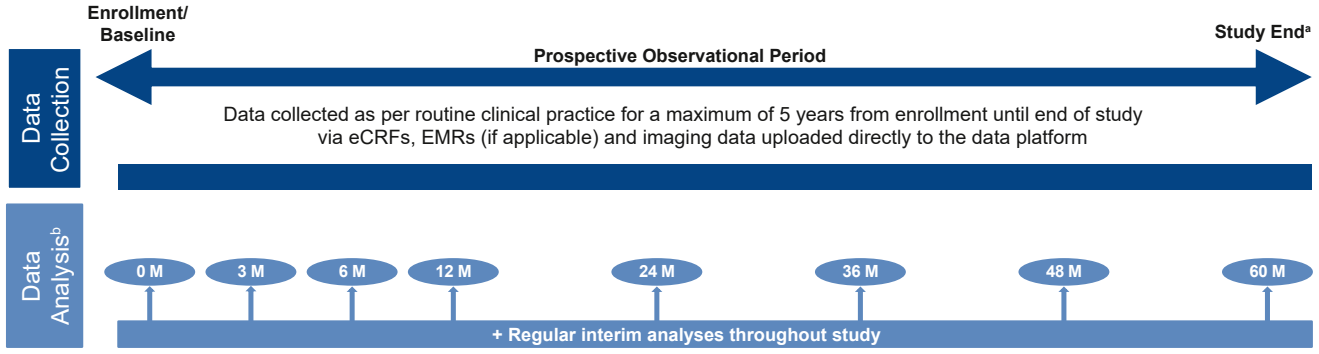

Figure 2. Study design schema. [a]Study end: Study completion or end of termination defined as death, loss to follow-up, withdrawal of consent, participation in an investigational ophthalmology clinical trial, early termination of the study, or discontinuation of the study site, whichever occurs first. [b]Data will be analyzed at specified time points (e.g., 3, 6, 12, 24, 36, 48, and 60 months with an appropriate window period of ±30 or ±60 days, etc.), for a maximum of approximately 5 years from study entry until study completion/early termination. eCRF = electronic case report form; EMR = electronic medical record; M = months.

disorganization of the retinal inner layers) on VA outcomes at months 3, 6, 12, and annually thereafter and according to treatment regimen and philosophies.

The safety objective is to evaluate ocular and systemic safety and tolerability of faricimab and PDS in the clinical practice setting. Nonocular adverse events (AEs) will be assessed at patient level. Ocular AEs will be assessed at eye level per approved retinal indication and product.

A complete list of objectives and end points is provided in Table 1.

Variables Collected

A full list of variables to be collected is outlined in the supplementary material (Table S2, available at www.ophthalmologyscience.org). All measurements will be collected per routine clinical practice and recorded on electronic case report forms (eCRFs) or obtained from electronic medical records. There will be no mandated study visits or imaging protocol requirements; however, ocular images will be collected when they are available. Visual acuity will be collected as per usual practice and automatically converted to approximate ETDRS letters in the eCRF.[30] Data on both eyes will be collected, irrespective of disease status and administered treatments.

Clinicians will be required to record all case details of serious AEs (SAEs), AEs of special interest, and serious adverse device effects in the eCRF and report these within 24 hours via an electronic data capture system. Nonserious AEs will be recorded in the eCRF and reported within 30 days of the event.

VOYAGER Ecosystem/Interface

Data from VOYAGER will be used to create an innovative and unique ecosystem that aggregates key data elements from the study to provide a holistic assessment of the clinical practice patient response (Fig 3). Patient data will be entered directly via eCRFs and/or will be automatically transferred over from existing electronic medical records at selected sites. All images will be standardized and sent and stored in the Roche Imaging Platform with the ability to link to clinical data stored in the database. Images will be analyzed in a separate analysis. The VOYAGER Ecosystem includes an innovative real-time digital interface designed to allow the graphical display of relevant information collected during the patient treatment journey. Longitudinal patient data will be displayed on one screen, including VA changes over time, treatment intervals, and presence and location of key features that are used to determine disease activity (e.g., fluid, hemorrhage and central subfield thickness) and those that impact vision (e.g., development of atrophy, fibrosis, and disorganization of retinal inner layers). Change from baseline and time of last active disease will be shown in a drop-down box to enable a rapid, yet comprehensive, analysis of the individual patient response to help inform future treatment decisions.

Statistical Methods

No formal sample size calculation linked to hypothesis testing has been done for this study. The study aims to enroll $\geq$ 5000 patients to have a sufficient number for analysis of study cohorts (faricimab in nAMD, faricimab in DME, and PDS in nAMD) and subgroups by region, baseline characteristics, and other factors. For mean change from baseline in VA (approximate ETDRS letter score) at 12 months, the 95% confidence intervals of the mean by number of eyes were calculated assuming an estimated standard deviation of $\leq$ 14.4 letters based on a meta-analysis of clinical practice studies reporting data for patients with nAMD or DME.[7,31–34] Due to the exploratory study design, yearly interim analyses and several subgroup analyses will be performed, and thus, in general, samples of up to 1000 eyes can be expected. For samples of 500 or 1000 eyes, the precision of the 2-sided 95% confidence interval is 1.3 or 0.9 letters, respectively, which is within an acceptable range.

Unless otherwise specified, analyses will be performed per study cohort (faricimab in nAMD, faricimab in DME, and PDS in nAMD). Missing data will not be imputed. Effectiveness analyses will be conducted using data from the Effectiveness Analysis Set (all patients who provide informed consent, fulfill all eligibility criteria, and have VA data available for the baseline visit and $\geq$ 1 postbaseline visit).

For the primary end point, actual values at baseline and month 12 and change from baseline in VA (approximate ETDRS letter score) at month 12 will be summarized descriptively per cohort. To evaluate specified outcomes over time, timepoints of interest will be defined (e.g., 3, 6, 12 months, and annually thereafter using the nearest visit relative to the defined timepoint). Patient demographics and medical history, baseline ocular characteristics and prior ocular treatments, and treating clinician's practice characteristics will be summarized. Patient disposition and number of treated eyes will be summarized overall and for each product by cohort in the Safety Analysis Set (patients who received $\geq$ 1 dose of study drug for their approved indications). Continuous variables will be summarized descriptively using mean, median, standard deviation, first quartile, third quartile, minimum, and maximum. Categorical outcomes will be summarized using numbers and percentages in each category. Corresponding 95% confidence intervals will be calculated if applicable.

The incidence of AEs and SAEs will be summarized descriptively by Medical Dictionary for Regulatory Activities primary System Organ Class and Preferred Term for the Safety Analysis Set. Cumulative AE and SAE incidence and rates per 100 patient-years will be calculated. The number and percentage of patients (or eyes) experiencing AEs and SAEs and the number of events will be displayed by System Organ Class, Preferred Term, and severity. Adverse events outcomes and duration will be summarized descriptively. Ocular AEs of special interest include intraocular inflammation.

Retinal images will be analyzed using advanced analytic tools (including machine learning and deep learning) in a separate analysis. Image analysis will be, in large part, via automated algorithms, which will take into consideration the different instruments and protocols involved in generating the images.

Subgroup analyses will evaluate outcomes by factors such as baseline VA, previous anti-VEGF treatment (treatment-naive, previously treated, switching treatment, or rolling over from a Roche interventional trial), fluid presence, and treatment (e.g., regimen and number) as well as by geographic region, practice type, and clinician philosophies (e.g., fluid tolerance and treatment end point) and experience (Table S3, available at www.ophthalmologyscience.org).

The final analysis will be conducted after the last patient has exited the study. No formal confirmatory effectiveness or safety interim analyses are planned. Exploratory interim analyses of selected end points are planned to be performed annually or semiannually (depending on available data).

Study Status

Enrollment began in November 2022. At the time of writing, the United States, Japan, and Canada had commenced enrollment, with more countries expected to initiate recruitment through 2023 and 2024.

Discussion

VOYAGER is a novel clinical practice study designed to explore the long-term effectiveness and safety of faricimab

Table 1. Study Objectives and End points

Primary Effectiveness Objective • To evaluate the effectiveness of specified Roche ophthalmology products for approved retinal indications on VA at 12 mo in the clinical practice setting	**Primary Effectiveness End Point** • Change in VA (approximate ETDRS letter score*) from baseline at month 12
Secondary Effectiveness Objectives • To evaluate the effectiveness of specified Roche ophthalmology products for approved retinal indications on VA at specified intervals during the conduct of the study, in the clinical practice setting • To describe retinal treatment regimens in the clinical practice setting	**Secondary Effectiveness End Points** • Change in VA (approximate ETDRS letter score*) from baseline at months 3, 6, 24 and annually thereafter • Number and percentage of eyes in each treatment regimen (i.e., fixed regimen, T&E, PRN, and other) • Number and percentage of treatments per year • Time spent on each treatment, overall and per regimen (i.e., fixed regimen, T&E, PRN, and other) • Number and percentage of eyes with treatment switch and reason for switch at 3, 6, 12 mo and annually thereafter • Total number of visits, number of visits with or without treatment, and time interval between treatments • Number, type, and frequency of ocular concomitant and subsequent medications received during the study period
• To evaluate the correlation between clinical practice regimens and change in VA over time	• Change in VA (approximate ETDRS letter score*) from baseline at months 3, 6, 12, and annually thereafter, according to the: o Treatment regimen (fixed, T&E, PRN, and other) o Number of treatments o Total number of visits o Treatment schedule
Safety Objective • To evaluate the ocular and systemic safety and tolerability for specified Roche ophthalmology products approved in retinal indications in the clinical practice setting	**Safety End Points** • Incidence, severity, duration, and outcome of ocular and nonocular adverse events
Exploratory Objectives • To describe changes in VA over time in relation to presence of fluid, treatment regimen, and treatment philosophies	**Exploratory End Points** • Changes in VA (approximate ETDRS letter score*) from baseline at months 3, 6, 12, and annually thereafter for eyes in each fluid group (no fluid, SRF, IRF, both SRF and IRF) and location and according to the treatment regimen and declared treatment philosophy (fluid tolerance)
• To evaluate changes over time in the proportion and location of anatomic features† and presence of fluid, as determined by clinical imaging assessments, in relation to the number of treatments, treatment regimen, treatment philosophies, and investigator-determined disease activity	• Anatomic features† and presence of fluid in relation to the number of treatments, treatment regimen, treatment philosophies and investigator-determined disease activity: o Proportion of eyes with presence/absence of IRF, SRF, and both IRF and SRF over time o Change in SRF/IRF from baseline over time *Note: specific end points for nAMD and DME are provided below under additional nAMD- and DME-specific end points*
• To evaluate changes in VA over time in relation to anatomic features† and presence of fluid	• Change in VA (approximate ETDRS letter score*) from baseline at months 3, 6, 12, and annually thereafter in relation to the presence and location of anatomic features† and fluid
• To evaluate the effectiveness of specified Roche products approved in retinal indications on CST reduction	• Change in CST from baseline at months 3, 6, 12, and annually thereafter (as measured per local standard clinical practice)
• To evaluate the effectiveness of specified Roche ophthalmology products approved in retinal indications on additional outcomes in the clinical practice setting	• Number and proportion of eyes, over time, with approximate ETDRS letter score* of: o ≥ 70 (20/40 Snellen equivalent) o 36 to 69 (between 20/40 and 20/200 Snellen equivalent) o ≤ 35 (20/200 Snellen equivalent) o Proportion of eyes gaining ≥ 15, ≥ 10, ≥ 5, or > 0 letters in VA* from baseline over time o Proportion of eyes losing ≥ 15, ≥ 10, ≥ 5, or > 0 letters in VA* from baseline over time

• To evaluate retinal fluid, anatomic parameters, and novel imaging biomarkers from ocular images using advanced analytics tools, machine learning, and deep learning[‡]	• Correlation between retinal fluid volume, fluctuations, and visual outcomes, using ocular images taken as per routine clinical practice[§]
• Additional nAMD-specific end points	• Number and percentage of eyes: o Reported by the investigator as having active disease, over time o With each nAMD subtype o With presence/absence of atrophy and location,[‖] at baseline, at months 3, 6, 12, and annually thereafter o With presence/absence of fibrosis and location,[¶] at baseline, at months 3, 6, 12, and annually thereafter o With presence/absence of SHRM at baseline, at months 3, 6, 12, and annually thereafter o With presence/absence of hemorrhage, at baseline, at months 3, 6, 12, and annually thereafter • Change in presence/absence and severity of PED from baseline at months 3, 6, 12, and annually thereafter
• Additional DME-specific end points	• Number and percentage of eyes reported by the investigator as having active disease, over time • Number and percentage of eyes by diabetic retinopathy severity level, at baseline, at months 3, 6, 12, and annually thereafter • Number and percentage of eyes with the following, at baseline, at months 3, 6, 12, and annually thereafter: o Noncentral or central involvement o Laser scars o HMA o Lipid exudates o DRIL o HRF

CST = central subfield thickness; DME = diabetic macular edema; DRIL = disorganization of retinal inner layers; eCRF = electronic case report form; HMA = hemorrhages and microaneurysms; HRF = hyperreflective foci; IRF = intraretinal fluid; nAMD = neovascular age-related macular degeneration; PED = pigment epithelial detachment; PRN = pro re nata; SHRM = subretinal hyperreflective material; SRF = subretinal fluid; T&E = treat-and-extend; VA = visual acuity.
*Approximate ETDRS letter score automatically converted to approximate ETDRS letters in the eCRF.[28]
[†]Anatomic features: fibrosis, atrophy, DRIL, and diabetic retinopathy severity.
[‡]This objective will use imaging data collected in this study but be analyzed separately.
[§]OCT images (spectral-domain or swept-source) taken as per routine clinical practice for the specified indications in scope for this study will be pseudoanonymized and uploaded into the vendor imaging management platform, and other images taken as per routine clinical practice (e.g., fundus color images, fundus fluorescein angiography, indocyanine green angiography, and OCT angiography, with this preferential order) may also be collected for the specified indications in scope for this study, whenever available. All images will be converted into standardized format and will be sent and stored in the Roche Imagining Platform with the ability to link to the clinical data stored in the research database.
[‖]Atrophy definition: usually defined as loss of photoreceptors and retinal pigment epithelium, atrophy is to be assessed as per the treating clinician.
[¶]To be assessed as per the treating clinician.

and PDS for the treatment of nAMD and DME. The overall goal is to optimize global treatment outcomes by gaining insights into the factors that contribute to outcomes in clinical practice studies. Collecting data on treatment regimens and philosophies as well as key anatomic features that impact VA should provide missing evidence to understand and start to address the discrepancy between clinical practice and clinical trial outcomes. The methodologies used in this study will ensure high internal and external validity.

Although there are disease registries and clinical practice studies that examine the outcomes of anti-VEGF treatment in retinal disease, data have generally been limited to VA and injection frequency, with few studies providing in-depth imaging analyses and assessment of reasons for management decisions.[24] Furthermore, although clinical practice studies[20] historically tend to be longer than clinical trials,[19] few are multinational and reflect heterogenous treatment environments,[24] limiting the ability to assess particular variables that impact long-term treatment effectiveness. These limitations mean a paucity of data exist regarding clinical practice treatment patterns (beyond injection frequency), anatomic features that impact visual outcomes, and other clinician- and disease-related characteristics that have an impact on treatment outcomes.

VOYAGER has a prospective study design and uses uniform data collection methods to ensure standardized data are collected. The study has a planned enrollment of $\geq$ 5000 patients to allow for subgroup analyses. Study length allows up to 5 years of follow-up, thereby providing long-term data. The broad eligibility criteria allow for inclusion of a diverse patient group more representative of routine care than the selected patient groups included in the pivotal nAMD and DME trials. Inclusion of study sites that are not all experienced with clinical trials from both regional and

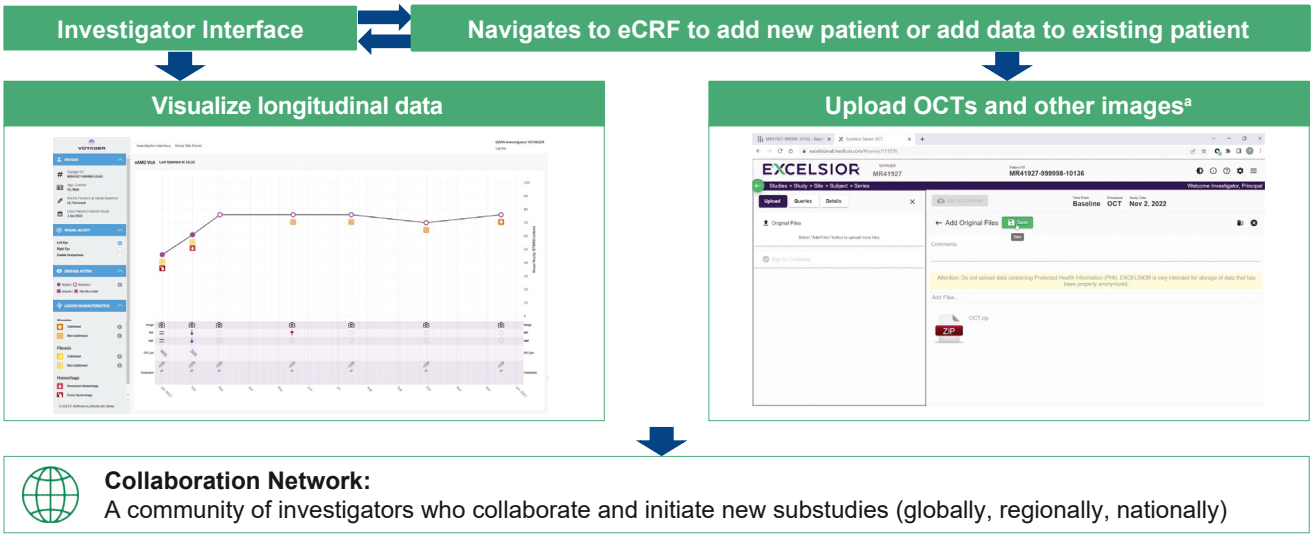

Figure 3. The VOYAGER Ecosystem. [a]Images collected for future artificial intelligence (AI) analytic tools and assessments include: color fundus photography, fundus fluorescein angiography, indocyanine green angiography, spectral-domain OCT, spectral-domain OCT angiography, swept-source OCT, and swept-source OCT angiography. eCRF = electronic case report form.

remote areas from across 31 countries will reflect diverse clinician experience and practice settings globally, allowing for wide generalizability of study results and in-depth understanding of factors that contribute to different outcomes.

VOYAGER is a novel prospectively designed clinical practice study that will comprehensively analyze how a range of treatment-, clinician-, and disease-related factors impact outcomes in both nAMD and DME. The correlation between clinical practice regimens and VA change over time will be assessed. Clinician interpretation of key imaging features and their determination of disease activity will be collected and assessed in relation to treatment decisions and VA outcomes. The importance of parameters to determine disease activity, such as the presence and location of fluid relative to the fovea, remains controversial, with some clinicians tolerating a degree of fluid in the subretinal space, while others aim for a dry retina despite long-term stable fluid. Asking clinicians their treatment philosophies, how they interpret scans, and how these interpretations impact their treatment decisions will provide insights into variations in clinical practice. Additionally, having access to a multimodal set of retinal images from VOYAGER will allow validation of certain key anatomic lesions, correlation of anatomic lesions with clinical interpretation, and their impact on visual outcomes. The large imaging repository will be available for further development of advanced analytical tools to allow processing of the imaging data.

The VOYAGER Investigator Interface will provide a graphical representation of the patient data collected, displaying the patient treatment journey and including key features that impact treatment decisions and VA outcomes on one screen. Clinicians see an individual patient's journey with clear icons and drop-down boxes that summarize key changes, which provides a comprehensive overview of the data to help make more informed treatment decisions. Additionally, the VOYAGER Ecosystem created from all recorded data creates the ideal setting to allow the VOYAGER collaboration network of investigators to delve into the data to explore new questions and initiate new substudies. A limitation of this study is that the results may not be replicable outside of this study where clinicians do not have access to the VOYAGER Investigator Interface or other summary data.

In conclusion, VOYAGER is an innovative study that will evaluate long-term vision outcomes and safety of faricimab and PDS for the treatment of nAMD and DME in routine clinical practice at global and regional levels. Through focused research questions and collection of data not usually captured by clinical practice studies, VOYAGER is ideally positioned to identify novel and potentially addressable factors affecting outcomes. The novel investigator interface will provide clinicians with a holistic picture of each patient's disease evolution over time to help inform treatment decisions. The data collected in VOYAGER will be critical to helping close the gap in outcomes between clinical practice studies and clinical trials and ensuring optimal long-term outcomes for patients with nAMD and DME globally.

Footnotes and Disclosures

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HUMAN SUBJECTS: Human subjects will be included in this study. Patient enrollment will be initiated after approval by institutional review boards/ethics committees. The study will be conducted in accordance with the Guidelines for Good Publication Practice, and local laws and regulations as applicable. Written informed consent will be obtained before any data are collected. All research will adhere to the tenets of the Declaration of Helsinki.

No animal subjects will be used in this study.

Author Contributions:

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Analysis and interpretation: Guymer, Bailey, Chaikitmongkol, Chakravarthy, Chaudhary, Finger, Gallego-Pinazo, Chuan, Ishida, Lövestam-Adrian, Parravano, Luna Pinto, Schmitz-Valckenberg, Sheth, Souied, Chi, Gilberg, Glittenberg, Scheidl, Bengus

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Abbreviations and Acronyms:
AE = adverse event; **DME** = diabetic macular edema; **eCRF** = electronic case report form; **nAMD** = neovascular age-related macular degeneration;

PDS = Port Delivery System with ranibizumab; **SAE** = serious adverse event; **VA** = visual acuity.

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