aHUS Registry Scientific Advisory Board (SAB) Charter

Alexion Pharmaceuticals, Inc.

Protocol Number M11-001 (aHUS Registry)

AN OBSERVATIONAL, NON-INTERVENTIONAL, MULTI-CENTER, MULTI-NATIONAL STUDY OF PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS)

Version: 2.0
Date: 24 February 2017

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1 Objectives

The Scientific Advisory Board (SAB) is a collaborative scientific board and advocacy group for the aHUS Registry (Alexion Pharmaceuticals Protocol number M11-001). Its role is to review and provide feedback on clinical assessments and patient outcomes collected in the aHUS Registry, to raise awareness and communicate the value of the Registry, to ensure suggested topics for analysis are in line with existing medical evidence needs, to confirm analysis methodologies are scientifically sound and relevant to the treating community, and to provide important perspectives to support analysis of data and interpret the study's findings.

2 Members

The membership of the SAB for the aHUS Registry will include those listed below.

2.1 SAB Members

Name	Country	Institution
Christoph Licht	Canada (Chair)	The Hospital for Sick Children and University of Toronto
Véronique Frémeaux-Bacchi	France (Co-chair)	Hôpital Européen Georges Pompidou, Paris
Gema Ariceta	Spain	Hospital Valle d'Hebron, Barcelona
Gianluigi Ardissino	Italy	Fondazione IRCCS Cá Granda, Ospedale Maggiore Policlinico, Milan
David Cohen	US	Columbia University, New York
Fadi Fakhouri	France	CHU de Nantes-Hôpital Hotel Dieu, Nantes
Larry Greenbaum	US	Emory University, Atlanta
Nicole Isbel	Australia	Princess Alexandra Hospital, Brisbane
Sally Johnson	UK	Newcastle Upon Tyne Hosptial, Newcastle
Franz Schaefer	Germany	University Clinic Pediatric Nephrology, Heidelberg
Marie Ann Scully	UK	University College London Hospitals NHS Foundation Trust, London
Johan Vande Walle	Belgium	UZ Gent Dienst Pediatrische Nefrologie, Gent
Leonard Woodward	UK	aHUS Alliance (Patient Advocate)
Ogawa, Masayo	US	Alexion Pharmaceuticals, Inc., New Haven
Gasteyger, Christoph	Switzerland	Alexion Pharma EMEA GmbH, Zürich

2.2 Membership Guidelines

Members of the SAB must have demonstrated expertise in aHUS. Membership should include representatives from key specialties managing aHUS patients whenever possible (e.g. adult and pediatric nephrologists, hematologists, transplant nephrologists/surgeons, genetics expert), patient advocate(s) as well as representation from Alexion Pharmaceuticals. It is considered preferable, however, to maintain the membership equilibrium between pediatric and adult nephrologists.

The term of membership is 4 years and a member may serve more than one term. Members will be asked if they are interested in continued membership on the fourth anniversary of their term. However, members have the right to terminate their

membership at any time by notifying the SAB Chair and/or Co-chair as well as Alexion Pharmaceuticals. It is requested that departing members commit to completion of ongoing projects where possible or agree to no longer be involved.

It would be counter-productive to have many SAB members leave at the same time. Within the terms noted membership turnover should be limited to 50% at any one time or to allow change by natural attrition.

As the aHUS Registry is a long-term commitment, it may be necessary to alter the membership of the SAB. A new SAB member can be proposed following either of two mechanisms at the discretion of the SAB itself:

- Replacement of a member who leaves the SAB
- Addition to the SAB of a member from an unrepresented region/country where a significant number of patients have been enrolled in the aHUS Registry

Any member of the SAB can recommend a potential candidate to the SAB Chair and/or Co-chair as well as Alexion Pharmaceuticals. New members will be approved by common agreement between all members. The SAB will be open to new members based upon SAB recommendations.

All members of the SAB will elect a Chair and a Co-Chair among the aHUS Experts. Representatives from Alexion Pharmaceuticals cannot be elected as Chair and/or Co-Chair. The Chair and Co-Chair will keep their position for a term of four years and he/she may serve more than one term with a maximum of two terms.

Elections of Chair and Co-Chair will take place at SAB meetings or via an electronic email or web-based voting mechanism. Term will start at the meeting where results are announced.

Active participation and attendance at SAB meetings is expected by all members. Failure to meet the requirements set forth in Sections 3.1 and 4.1 may result in a member being replaced as described above. This will be strongly enforced by the SAB Chair and Co-chair.

All SAB members have one vote each. The SAB Chair has the decisive vote if a voting stands 50:50. Topics requiring a vote will be specified in the meeting agenda. Voting can be done in at a meeting or electronically.

2.3 Patient Advocacy Representative

A patient advocate will be invited to participate. The patient advocate will participate for a period of four years from the time they join the committee. There will be one meeting overlap when a new patient advocate or advocacy group and the past patient advocacy representative are both invited to participate.

They may participate in meetings under the following guidelines:

- Patient advocacy representatives will sign an agreement that details their roles and responsibilities, including participation in meetings, and logistical arrangements such as travel compensation.
- The advocacy representatives must be active members of the advocacy group they are representing and should serve as a delegated representative of their advocacy group.
- It is important to consider how patient advocacy representatives/groups wish to interact with the SAB. This is subject to change with the advocacy group.

Patient advocate representatives will be non-voting members of the SAB.

3 Roles and Responsibilities

3.1 SAB members

The SAB is a collaborative scientific board and an advocacy group for the aHUS Registry. Its role is to review data collected in the aHUS Registry database, to provide important expert perspectives to support analysis of the results, and to review and respond to aHUS Registry Investigator requests.

SAB members will be responsible for the following activities associated with the aHUS Registry:

SCIENTIFIC ADVICE

- Provide scientific advice on aHUS Registry-related matters
- Propose, discuss and evaluate program objectives with Alexion Pharmaceuticals
- Review and provide guidance on future amendments to the protocol, as appropriate
- Review and provide guidance on data variables to be collected, case report form refinements, and reports as appropriate
- Provide *ad hoc* review of documents and periodic phone/email consultation

PUBLICATIONS

- Advise on analyses and scientific questions of interest
- Review and provide feedback on publication goals and logistics
- Contribute to publication plan

- Establish criteria for review and approval of external requests for analyses and publications (e.g. requests from individual investigator or National Coordinator)
- Review publication drafts before submission to journals or public release
- Advise, counsel, and guide individuals on publications that utilize aHUS Registry data and resources and/or use the aHUS Registry name

ADVOCACY

- Generation of program awareness and interest in members' medical community
- Assist with involvement of professional associations, support groups, and patients as appropriate
- Welcome and encourage collaborative research in aHUS
- Contribute to a plan to drive communications (newsletters, press releases, etc.) to external audiences
- Serve as resource to Alexion Pharmaceuticals and sites for operational questions

3.2 SAB Chair

The SAB Chairperson will have the following additional specific roles and responsibilities:

- Serving as primary contact with Alexion Pharmaceuticals for all topics related to the SAB
- Defining each meeting agenda together with Alexion Pharmaceuticals
- Leading each SAB meeting in conjunction with Alexion Pharmaceuticals
- Reviewing and validating the minutes of each meeting

3.3 SAB Co-Chair

The SAB Co-Chairperson will have the following additional specific roles and responsibilities:

- Consulting with the Chair on major SAB decisions and responsibilities
- Supporting the Chair in his/her role serving as the primary contact with Alexion Pharmaceuticals for all topics related to the SAB
- Assisting the Chair with defining each meeting agenda together with Alexion Pharmaceuticals
- Leading SAB meetings in the Chair's absence in conjunction with Alexion Pharmaceuticals
- Assisting the Chair with reviewing and validating the minutes of each meeting

3.4 Patient Advocacy Group representative

The patient Advocacy group representative will have the following responsibilities:

- Provide advice on aHUS Registry-related matters
- Propose, discuss and evaluate program objectives with Alexion Pharmaceuticals
- Provide *ad hoc* review of patient-related documents
- Advise on analyses and scientific questions of interest to the patient community

- Generate program awareness and interest within the patient community
- Assist with involvement of patient, support groups, and patients
- Provide information on the aHUS Registry to physicians and patients
- Provide advice and support to patients participating in the study
- Act as the interface with other patient advocacy groups to provide a broad patient perspective from multiple countries

3.5 Operational Team

The Operational team consists of representatives Alexion Pharmaceuticals members from Clinical Operations (US & EU), Epidemiology/Biostatistics, Pharmacovigilance and Scientific Communication.

4 Meetings

4.1 Meetings

SAB members agree to participate in two face-to-face meetings per year. If necessary, special arrangements can be made for teleconferences and/or webcasts. *Ad hoc* meetings may take place as teleconferences and/or webcasts as appropriate.

- Attendance at the meetings is expected. If an SAB member fails to participate in two meetings consecutively, the SAB Chair or Alexion Pharmaceuticals may contact the SAB member and discuss their future participation in the SAB. The SAB member could be replaced by the SAB Chair via the process described above in Section 2.3.

- Each meeting will be preceded by a written agenda sent to all SAB members at least one week prior to the meeting. Agendas will be validated by the SAB Chair prior to distributing to all SAB members. Issues that are raised for discussion by any member of the SAB or any physician participating in the aHUS Registry will be included.

- Each meeting will be followed by written minutes sent to all SAB members within three weeks after the meeting. Minutes will be validated by the SAB Chair.

5 Data Access, Publications Rules

5.1 Data Access

Access to the aHUS Registry database will be based on the following guidelines:

- SAB has access to the global database and will be involved in review of requests from physicians for analyses of global dataset, via Concept Sheets.
- National Coordinators will receive and have access to their country data, upon request. Additionally, they may request global data from the SAB.

- Individual participating physicians can access their own data at any time. They can request access to national data through the National Coordinator (NC) or global data through the SAB. Non-participating physicians can also submit a request to the SAB for analysis consideration, via Concept Sheet.
- As a courtesy, the SAB should be informed of all data requests.
- Data will be returned to individual investigators on cessation of the Registry.

Alexion Pharmaceuticals is responsible for:

- Managing and maintaining the study database
- Generating and distributing standard reports upon request as follows:
    - Individual sites have immediate access to their own site level data and general information on global registry/country/region, upon request
    - National Coordinators will receive Standard Country Reports, upon request
    - SAB members will receive reports from the global database, upon request
- Responding to *ad hoc* requests for data via Concept Sheets following consultations with the SAB
- Generating and submitting annual updates to relevant regulatory authorities
- Safety Reporting – regular reporting and signal detection analyses
- Responding to *ad hoc* requests from regulatory agencies (FDA, EMEA, Australia, Japan, etc.)

5.2 Publications

The SAB, in conjunction with Alexion Pharmaceuticals, will define a plan for regular publications based on analysis of global registry data, including the contents of such publications. Publications include manuscripts submitted to peer-reviewed journals, along with abstracts submitted to scientific conferences and subsequent conference poster/presentational materials. For each publication, the SAB and Alexion Pharmaceuticals will work together to develop working groups who will have the primary responsibility for actively taking part in guiding data analyses, interpretation of data analyses, and for the publication writing. Membership of working groups will consist of aHUS experts and SAB members, as defined in the M11-001: aHUS Registry Authorship Criteria Process document.

Working groups will be composed of some SAB members and/or other aHUS experts, and should not exceed a total of ten (10) participants.

5.3 Ad hoc requests for analyses/publications

The SAB is responsible for reviewing publication proposals, analysis requests, and identifying journals, venues, and audiences of interest. Any physician may publish data analysis based on his/her own patient using their own resources and any physician, including those not participating in the study, may submit analysis requests for consideration to support a publication, via Concept Sheets. The SAB will evaluate the scientific merit of the analysis request and the alignment with the Registry publication strategy. Prioritization of publication will be based on academic/scientific importance of the questions and the source of the request (i.e., study investigator, National

Coordinator, non-investigator). Complexity of analyses and potential for overlapping or conflicting analyses will be evaluated during *ad hoc* or face-to-face SAB meetings and feedback will be provided to requesters after the meeting. The SAB may recommend combining similar requests for analyses and publications. Contributing investigators need to agree to publication. Proposed authorship will be included as criteria for proposal evaluation and selection, with the goal of ensuring equity in authorship

National Coordinators analyzing their country data independently may publish without SAB approval but if registry operational resources are required to be provided then a request should be made to the SAB for prioritization against other requests and projects, even though not utilizing global data. As a courtesy, the SAB should be informed of data to be published on aHUS Registry data.

A publication proposal on global data should be submitted to the operational team for distribution to the SAB, via Concept Sheet. All requests will be centralized by the operational team for ease of tracking, forwarded to the SAB and presented at the next SAB meeting for discussion, prioritization, and voting, if applicable. After the SAB meeting, the Operational Team will be responsible for communicating the decision to the requesting physician(s), and liaising with him/her for all further actions, as needed.

Prior to submission for publication of any manuscript, poster, presentation, abstract or other written or oral material describing the results of the Registry, the SAB and Alexion Pharmaceuticals shall have thirty (30) calendar days to review a manuscript and fifteen (15) calendar days to review any poster or PowerPoint presentation, abstract or other written or oral material which describes the results of the Registry. If Alexion Pharmaceuticals requests in writing, the physician shall withhold any publication or presentation an additional sixty (60) calendar days solely to permit Alexion Pharmaceuticals to remove any Confidential Information. Any physician may, without restriction, publish an analysis of data from their own subjects (and not from the aggregate) that are contributed to the Registry database consistent with the terms and conditions of the informed consent/authorization and applicable law. As a courtesy, the SAB should be informed of data to be published on aHUS Registry data.

5.4 Reports to Health Authorities

For any report required by any health authority, Alexion Pharmaceuticals will be solely and entirely responsible for conducting the data analyses and writing of such report, without involving the SAB. Such a report may concern data from one single region or country or overall data.

6 Consulting Agreement

SAB members agree to provide consulting services via participation in the aHUS Registry Scientific Advisory Board (SAB); services shall be performed at such times as they will not interfere/be in conflict with your obligations to any institution(s) with which you are affiliated.

SAB members further agree that any tangible property provided to physicians in connection with the aHUS Registry, including all data, reports, or other information generated under the aHUS Registry (and any inventions or other results of such data, reports, or other information) shall be and remain the exclusive property of Alexion Pharmaceuticals.

6.1 Honoraria

It is expected that SAB members' involvement will require approximately 50 hours per year (travel included). The SAB Chair and Co-Chair will likely expend approximately 70 hours per year.

Financial conditions to compensate this will be specified in an agreement executed with each SAB member.

7 Operating Principles

SAB members agree to serve as an independent contractor (to Alexion Pharmaceuticals); nothing in this Charter shall be construed in any manner as an obligation or inducement for SAB members to recommend that patients utilize Alexion Pharmaceuticals' products or those of any organizations affiliated with Alexion Pharmaceuticals.

8 Confidentiality and Nondisclosure

SAB members agreeing that all non-public information (disclosed by Alexion Pharmaceuticals or becoming known to you as a result of serving on the SAB) is confidential and shall not be disclosed.