Endorsed by the ICH Management Committee on 12 May 2023

ICH Remit Paper

ICH Cell and Gene Therapies Discussion Group

General Description

The ICH Cell and Gene Therapies Discussion Group (CGTDG) will serve as a technical discussion forum for issues related to ICH harmonization efforts in the field of Cell and Gene Therapies (CGT) products. The CGTDG will develop a holistic CGT roadmap within the scope of modalities identified below, including prioritization of areas of most need for harmonization whereby technical consensus can be achieved with specific recommendations for new guideline development or revisions to existing ICH Guidelines.

As acknowledged by the ICH Management Committee (MC), there is a developing need for regulatory harmonization on topics related to CGT products, an emerging field with an expanding global clinical development landscape and a significant promise in the treatment and cure of debilitating and life-threatening diseases. The overall aim of CGTDG is to develop a strategic framework to address the future harmonization needs for this emerging field, and provide recommendations to the MC in guiding ICH activities to address these technological advancements. It is expected that the ICH CGTDG will work in close collaboration and coordination with IPRP and WHO CGT focused groups to ensure a holistic approach to harmonization efforts, and equally minimize any duplicative efforts.

The CGTDG will operate in line with the applicable ICH procedures, similar to other ICH Discussion Groups, under the oversight of the ICH MC, and reporting to the ICH Assembly. As the remit of ICH is to harmonize technical standards, the CGTDG is tasked to focus on technical and scientific aspects and ensure that ICH Guidelines are kept up-to-date with the evolution of science.

Scope of Activities

Given the scientific complexities and diverse array of CGT modalities, it is proposed that the CGTDG focus its initial scope on CGT modalities of relatively high maturity, whereby greater scientific and regulatory expertise have already been achieved. The selection of such modalities can be linked to classes of products that have achieved global marketing authorization or those modalities that are prominent in global clinical development programs. The proposed modalities within scope are:

- Ex-vivo genetically modified chimeric antigen receptor engineered T cell (CAR-T cell), including both autologous and allogeneic;
- In-vivo viral vector-based gene therapy (e.g., AV, AAV, …).

The initial work of the CGTDG will be to drive alignment on high level principles within selected modalities where baseline consensus can be achieved. The CGTDG will:

- Review areas that will benefit from ICH harmonization, and prioritize those areas of most need to enable future ICH work in a staggered approach;
- Assess current ICH Guidelines for their applicability to CGT products, and;
- Make specific recommendations regarding the development of new ICH guidelines for CGT products and/or revisions to existing guidelines as deemed necessary.

The CGTDG is not tasked with the development or revisions of specific ICH Guidelines but may act as an advisor group to existing ICH Expert Working Group (EWG) undergoing new or revised guideline development where CGT products are in scope.

Given the diversity of the field and rapidly evolving science, the CGTDG should monitor innovation trends in clinical development and be given reasonable level of flexibility in adapting its work within the broader MC mandate. Significant changes to the overall scope should be presented to the MC for review and endorsement as per standard ICH procedures.

Type of Expertise Needed

The CGTDG should be comprised of a diverse group of strategically-oriented experts that collectively have extensive knowledge of the scientific and regulatory aspects of the selected CGT product modalities at all stages of development. The CGTDG expertise should overall be balanced across the non-clinical, clinical, and quality areas, with preferences for experts with high level expertise on the interfaces of non-clinical/clinical and quality disciplines. It is required that experts have some direct experience with the development and/or regulatory review of selected modalities.

It is envisioned that the CGTDG should be comprised of experts from Members and Observers of the ICH Assembly, in accordance with the applicable Assembly Rules of Procedure (ROP), MC ROP and Standard Operating Procedures (SOP) of the ICH Working Groups (WGs). ICH Members and Observers who desire to participate in the CGTDG will be allowed to nominate standing experts and alternate experts to enable an appropriate balance of expertise while keeping the size of the CGTDG manageable, in accordance with the applicable SOP.

Operating Model and Term

The CGTDG should complete its activities in a virtual setting via email and typically monthly teleconferences, as much as possible. It is, however, envisioned that the CGTDG may benefit from a face-to-face meeting at a suitable time during the course of the group proceedings, to accelerate the development of the strategic roadmap. The timing of such a meeting, as deemed necessary, should be determined by the group in conjunction with ICH regular proceedings (e.g., biannual ICH Meeting), and the granting of the meeting is at the discretion of the ICH MC. The leadership of the CGTDG should be comprised of a Rapporteur and a Regulatory Chair.

The CGTDG will operate with a 2-year term following the approval of its Remit by the ICH MC and the completion of the nomination process. The CGTDG should provide an update of its activities and progress biannually to the ICH MC and the ICH Assembly, in line with current practice for other ICH WGs.

In support of the CGTDG Scope of Activities outlined above, the CGTDG should endeavor to complete these interim milestones within the below suggested timeframe:

- Within the first 6 months: The CGTDG aims to have alignment on high level principles in key areas of select CGT modalities where baseline consensus can already be achieved;
- Within the first 12 months: The CGTDG will perform a stepwise review of existing ICH Guidelines with the aim to first identify areas where harmonization already exists, followed thereafter by determination of areas/opportunities for improvement;
- Within the first 24 months: The completion of a holistic CGT roadmap for modalities in scope, including prioritization of areas of most need for harmonization with specific recommendations for new guideline development or revisions to existing guidelines. Such

recommendations can be made at any appropriate timepoint during the proceedings of the group. As per ICH procedures, the actual topic proposals would be authored and submitted by ICH Member(s) following the ICH New Topics proposal process;

- The CGTDG will consider developing a paper summarizing the high-level principles, noted above, as well as the CGT roadmap, including prioritized areas for harmonization, for publication on the ICH website following ICH MC and Assembly review.