JUSTIFICATION FOR EARLY TERMINATION OF THE STUDY:

- **TITLE:** “Study of the effects of telomerase reactivation with Danazol on ovarian function. A Pilot Study”
- **EUDRACT NUMBER:** 2018-004400-19
- **PROMOTER'S PROTOCOL CODE:** 1707-FIVI-084-MV

This study (1707-FIVI-084-MV) has been terminated earlier due to several events that are explained below:

- The study protocol was written using a very "pure" design from the scientific point of view, with very strict inclusion and exclusion criteria. These criteria ended up reducing considerably the number of candidates that could have participated in the study.
- Many women did not participate because they had to be randomized to treatment or placebo and they did not like the idea of wasting three months if they were allocated to the placebo group. This point was particularly important for women with advanced age.
- There were long delays regarding the reception of the medicine (Danazol) as well as the placebo in the clinics, due to manufactures´ issues, which led to a considerable delay in the initiation of the study.
- Once patients´ recruitment had been initiated, which was going rather slowly (two patients in three months) the COVID-19 pandemic started, followed by the confinement of the population, which further delayed the recruitment of women. In addition, the follow up of women who had started the treatment before the lock down period was very complicated.
- Right after the lock-down period was over, the clinic started again to recruit women for the study, but the medicine/placebo had almost reached the expiration date, so we had to apply for an extension of the expiration date. In addition, we had to extend the insurance policy and the pharmacovigilance´s fees for one more year than stipulated at the beginning of the project. These extensions meant extra costs that had not been contemplated earlier.
- Another consequence of the lock down was that women who wanted to become pregnant did not want to wait any longer to achieve pregnancy because the lock down had already delayed their wish to become mothers.

All these factors have negatively influenced the evolution of the study by prolonging the recruitment time to a total of two years from the start of the study.

In addition to the above items, it should be added that the possibility of extending the study six more months (until the expiration date of the drugs under investigation) was considered in order to increase the number of women recruited per arm. However, this

would have meant a considerable increase in the costs without any guarantee of achieving the objective of the study (15 persons per arm).

Lastly, I would like to indicate that the final results obtained in this study will be uploaded in the corresponding websites of the Official Organizations for Clinical Trials before the end of December 2022.