Supplemental file 2

The ProFET trial – a complete list of secondary outcomes

1. Number of participants with biochemical pregnancy [Time Frame: 2-3 weeks after embryo transfer.]

   A pregnancy diagnosed only by the detection of beta hCG in serum or urine.

2. Number of participants with clinical pregnancy [Time Frame: 4-8 weeks after embryo transfer.]

   A pregnancy diagnosed by ultrasonographic visualization of one or more gestational sacs.

3. Number of participants with ongoing pregnancy [Time Frame: 5-7 weeks after embryo transfer.]

   An intrauterine pregnancy with one or more fetuses with heartbeats measured in gestational week 7+5 to 9+0 with vaginal ultrasound.

4. Number of participants with miscarriage [Time Frame: Up to 20 weeks after embryo transfer.]

   The spontaneous loss of an intra-uterine pregnancy prior to 22 completed weeks of gestational age. Also, the outcome will be reported according to Core Outcome Measure for Infertility Trials (Duffy et al., 2020) in a separate appendix.

5. Number of participants with ectopic pregnancy [Time Frame: Up to 20 weeks after embryo transfer.]

   A pregnancy outside the uterine cavity, diagnosed by ultrasound, surgical visualization, or histopathology.

6. Number of participants with termination of pregnancy [Time Frame: Up to 20 weeks after embryo transfer.]

Defined as the termination of a clinical pregnancy, by deliberate interference that takes place before 22 completed weeks of gestational age. Also, the outcome will be reported according to Core Outcome Measure for Infertility Trials (Duffy et al., 2020) in a separate appendix.

7. Birth weight [Time Frame: Up to 41 weeks after embryo transfer.]

   Defined as weight in grams at birth.

8. Gestational age at delivery [Time Frame: Up to 41 weeks after embryo transfer.]

   The gestational age at FET is calculated by adding the number of culture days to ovulation (ovulation=day 14). Gestational age at delivery is then calculated by adding the number of days since FET.

9. Preterm birth [Time Frame: Up to 35 weeks after embryo transfer.]

   Defined as a child born alive before 37 completed weeks of pregnancy.

10. Very preterm birth [Time Frame: Up to 30 weeks after embryo transfer.]

    Defined as a child born alive before 32 completed weeks of pregnancy.

11. Low birth weight [Time Frame: Up to 41 weeks after embryo transfer.]

    Birth weight less than 2500 g.

12. Very low birth weight [Time Frame: Up to 41 weeks after embryo transfer.]

    Birth weight less than 1500 g.

13. Stillbirth [Time Frame: Up to 41 weeks after embryo transfer.]

    The death of a fetus prior to the complete expulsion or extraction from its mother, after and including 22 completed weeks of gestational age. Also, the outcome will

be reported according to Core Outcome Measure for Infertility Trials (Duffy et al., 2020) in a separate appendix.

14. Perinatal death [Time Frame: Up to 41 weeks after embryo transfer and 7 days after birth.]

    Fetal or neonatal death occurring during late pregnancy (at 22 completed weeks of gestational age and later), during childbirth, or up to seven days after birth. Also, the outcome will be reported according to Core Outcome Measure for Infertility Trials (Duffy et al., 2020) in a separate appendix.

15. Number of children with birth defects [Time Frame: Up to 41 weeks after embryo transfer.]

    Congenital birth defects were defined according the International Statistical Classification of Diseases and Related Health Problems (ICD-10). And further defined according to the EUROCAT classification system.

16. Number of children admitted to Neonatal Intensive Care Unit (NICU) [Time Frame: Up to 41 weeks after embryo transfer and 7 days after birth.]

    Defined as children that were admitted to NICU after birth.

17. Number of participants with hypertensive disorders of pregnancy [Time Frame: Up to 41 weeks after embryo transfer including the postpartum period before discharge of mother.]

    Hypertensive disorders of pregnancy defined as high blood pressure disorders including preeclampsia, gestational hypertension and chronic hypertension.

18. Number of participants with placenta previa [Time Frame: Up to 41 weeks after embryo transfer.]

    Defined as a placenta covering the internal os of the cervix, at time of delivery.

19. Number of participants with placenta abruption [Time Frame: Up to 41 weeks after embryo transfer.]

Defined as the premature separation of a normally located placenta from the uterine wall that occurs before delivery of the fetus.

20. Number of participants with postpartum hemorrhage [Time Frame: Up to 41 weeks after embryo transfer.]

    Defined as a cumulative blood loss of greater than 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process.

21. Number of participants with Cesarean section [Time Frame: Up to 41 weeks after embryo transfer.]

    Defined as a surgical procedure used to deliver a baby through incisions in the abdomen and uterus.

22. Number of participants with thromboembolic events [Time Frame: Up to 41 weeks after embryo transfer including the postpartum period before discharge of mother.]

    Defined as formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the blood stream to plug another vessel.

23. Maternal mortality [Time Frame: Up to 41 weeks after embryo transfer including the postpartum period before discharge of mother.]

    Defined as female deaths from any cause related to or aggravated by pregnancy or its management (excluding accidental or incidental causes) during pregnancy and childbirth.

24. Number of participants with treatment related side effects [Time Frame: Up to 8 weeks after embryo transfer.]

    Side effects reported according to study specific questionnaire. Questions are answered with yes or no. If yes, symptoms are described, but not by using a scale.

25. Number of participants with adverse events [Time Frame: Up to 8 weeks after embryo transfer.]

Any untoward medical occurrence in symptom or disease temporally associated with the use of the medicinal (investigational) product, whether or not related to the medicinal product.

26. Cost effectiveness [Time Frame: After study completion, an average of 1 year.]

Comparison between groups regarding the total costs for the intervention divided by treatment efficacy (live birth).