OVERALL SYNOPSIS OF THE CLINICAL INVESTIGATION # 21E0787

ANSM registration #:	**2021-A02451-40**
Clinical investigation plan #:	**21E0787**
Title of the clinical investigation:	**Clinical study for the safety and effectiveness of use of an injectable medical device GANA V® for facial aesthetic treatment**
Sponsor:	**GCS Co., Ltd.** 1008 Ho, Sunil Technopia Bldg, 555 Dunchon-daero Jungwon-gu, Seongnam-si, Gyeonggi-do KOREA
Development phase	Post market study Interventional Device used according to Instruction For Use (IFU)
Objectives:	The primary objective is to evaluate the effectiveness of Gana V® in comparison with Sculptra® in the correction of Nasolabial Folds (NLFs) 6 months after treatment initiation. The secondary objectives of the study are: - To evaluate the effectiveness of Gana V® in comparison with Sculptra® in the correction of Nasolabial Folds (NLFs) $1^{1/2}$, 3, 9, 12, 18 and 24 months after treatment initiation. - To evaluate the effectiveness of Gana V® in comparison with Sculptra® on the global aesthetic improvement $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation. - To evaluate the effectiveness of Gana V® in comparison with Sculptra® in reducing NLFs depth and volume $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation. - To evaluate the subject satisfaction with Gana V® in comparison with Sculptra® $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation. - To evaluate the injector satisfaction with Gana V® in comparison with Sculptra® after initial injection and touch-up injection if applicable. - To evaluate the safety of Gana V® in comparison with Sculptra®.
Design:	The study will be: • double-blinded, • randomized, • within-subjects: each subject testing both devices, • versus comparator, • single centre.
Planned Sample Size:	55 subjects randomized.
Number of investigational study sites:	1 site (France)
Inclusion criteria:	1. Healthy Subject 2. Sex: male or female 3. Age: between 30 and 70 years. 4. Subject with moderate to severe nasolabial folds as determined by a Wrinkle Severity Rating Scale (WSRS) score of 3 or 4 on both folds at the pre-treatment evaluation.

	5. Subject wiling to abstain from other facial procedures (i.e., dermal fillers, toxin treatments, laser, microdermal abrasion, chemical peels, non-invasive skin-tightening) during the whole study period. 6. Subject, psychologically able to understand the study related information and to give a written informed consent. 7. Subject having given freely and expressly his/her informed consent. 8. Subject willing to have photographs of the face taken. 9. Subject affiliated to a health social security system. 10. Female of childbearing potential should use a contraceptive regimen recognized as effective since at least 12 weeks before screening visit and during the whole study period.
Exclusion criteria:	1. Pregnant or nursing woman or planning a pregnancy during the study. 2. Subject with a scar, moles, pigment disorders or anything on the face which might interfere with the evaluation. 3. Subject who had been deprived of their freedom by administrative or legal decision or who is under guardianship. 4. Subject in a social or sanitary establishment 5. Subject participation to another research on human beings or who is in an exclusion period of one. 6. Subject having received 4500 euros indemnities for participation in research involving human beings in the 12 previous months, including participation in the present study. 7. Subject suspected to be non-compliant according to the investigator's judgment. 8. Subject suffering from a severe or progressive disease or any other pathology that may interfere with the evaluation of the study results. 9. Subject with known history of or suffering from autoimmune disease and/or immune deficiency. 10. Subject suffering from inflammatory and/or infectious cutaneous disorders in or near the studied zones (e.g. acne, mycosis, papilloma, chronic eczema, atopic dermatitis…). Subject with labial herpes in the last 2 years is not eligible even if asymptomatic at time of screening visit. 11. Subject with an abscess, unhealed wound, or a cancerous or precancerous lesion on the studied zone. 12. Subject prone to develop inflammatory skin conditions or having tendency to bleeding disorders. 13. Subject with a tendency to develop keloids or hypertrophic scarring. 14. Subject having history of allergy or anaphylactic shock including hypersensitivity to Poly-l-lactic acid, to lidocaine or to one of the components of the tested devices or antiseptic solution. 15. Subject having received treatment with a laser, a dermabrasion, a surgery, a deep chemical peeling or other ablative procedure on the face within the past 12 months prior to screening visit. 16. Subject having received injection with a resorbable filling product in the face area within the past 12 months prior to screening visit. 17. Subject having received at any time injection with a slowly resorbable filling product (polylactic acid, calcium hydroxyapatite, combinations of hyaluronic acid (HA) and hypromellose, HA and dextran microbeads or HA and

	TriCalcium Phosphate (TCP), …) or with a non-resorbable filling product (polyacrylamide, silicone, combination of methacrylic polymers and collagen, polymer particles, …) on the face. 18. Subject having received at any time a treatment with tensor threads on the face. 19. Subject having started or changed her oral contraceptive or any other hormonal treatment during 12 weeks prior to screening visit. 20. Subject using medication such as aspirin, nonsteroidal anti-inflammatory drugs (NSAID) (ibuprofen, naproxen, …), antiplatelet agents, anticoagulants or other substances known to prolong bleeding time within 1 week prior to injection visits. 21. Subject undergoing a topical treatment on the test area or a systemic treatment: • Antihistamines during the 2 weeks prior to screening visit. • Immunosuppressors and/or corticoids during the 4 weeks prior to screening visit. • Retinoids during the 6 months prior to screening visit. 22. Intensive exposure to sunlight or UV-rays within the previous month before and after injection visits.
Investigational device: **Name / code** **Classification** **Composition** **Galenic form** **Administration route**	 Gana V® Class III medical device Poly-L-Lactic Acid (210mg), Sodium Carboxymethyl Cellulose, Mannitol. Sterile freeze-dried preparation (powder) Injection in the deep dermis and subcutaneous layer
Comparator: **Name / code** **Classification** **Composition** **Galenic form** **Administration route**	 Sculptra® Class III medical device Poly-L-Lactic Acid (150mg), Sodium Carboxymethyl Cellulose, Mannitol. Sterile freeze-dried preparation (powder) Injection in the deep dermis and subcutaneous layer
Endpoints:	<u>Primary effectiveness endpoint</u>: Mean change in NLFs severity from baseline to 6 months after treatment initiation, as assessed by an independent blinded live evaluator using the validated 5-point Wrinkles Severity Rating Scale (WSRS). <u>Secondary effectiveness endpoints:</u> - Mean WSRS change from baseline to $1^{1/2}$, 3, 9, 12, 18 and 24 months after treatment initiation as assessed by a blinded live independent evaluator. - WSRS responder rates $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation as assessed by a blinded live independent evaluator. A responder is defined as a subject with at least 1-point improvement from baseline on the WSRS. - Global Aesthetic Improvement Scale (GAIS) responder rates $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation as assessed by subjects and a blinded live independent evaluator. A responder is defined as a subject having

	"Improved", "Much improved" or "Very much improved" score according to GAIS. - Mean change in NLF depth and volume from baseline to $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation using fringe projection system. - Proportion of satisfied subjects $1^{1/2}$, 3, 6, 9, 12, 18 and 24 months after treatment initiation using a questionnaire. - Injector's satisfaction regarding injection quality after initial and touch-up injection using a questionnaire. <u>Secondary safety endpoints:</u> Investigational devices safety will be assessed by collection of Injection Site Reactions (ISRs) and Adverse Events (AEs) throughout the study by the investigator. Subjects will record ISRs and AEs in their subject diaries.
Study Procedures:	A screening visit will allow to inform and preselect the subjects. On D0, baseline scoring (WSRS), fringe projection acquisitions and photographs will be done before injection. Eligible subjects will receive a first injection of the investigational devices according to the randomization list. Immediately after injection, injector's treatment satisfaction will be collected. Investigator evaluator will collect Adverse Events (AEs) and Injection Site Reactions (ISRs) immediately after injection. A month and a half after initial injection ($M1^{1/2}$), WSRS and GAIS scoring, fringe projection acquisitions and photographs will be done before touch-up (if applicable). Subject's treatment satisfaction and injector's treatment satisfaction (if applicable) will be collected. A touch-up injection will be made if necessary, according to injector and subject opinion. Investigator evaluator will collect AEs and ISRs before and after touch-up if applicable. Three (M3), six (M6), nine (M9), twelve (M12), eighteen (M18) and twenty-four (M24) months after initial injection, effectiveness scoring (WSRS and GAIS scales), fringe projection acquisitions and photographs will be done. Subject's treatment satisfaction will be collected. Investigator evaluator will collect AEs and ISRs
Statistical methods:	**<u>For the primary evaluation criterion:</u>** The parameter Wrinkle Severity Rating Scale (WSRS) with the <u>5 level scores</u> (at D0 before injection and M6) will be summarized using statistics for quantitative variable (N, mean, median, standard deviation, first and third quartile, minimum and maximum value) for each timepoint as well as for the change from baseline (M6-D0bef) by product. **<u>Inferential analysis for the primary endpoint:</u>** The non-inferiority of Gana V® versus Sculptra® will be demonstrated if the upper-limit of the two-sided 95% CI of the (M6-D0bef) mean difference is inferior or equal to 0.5. **<u>For the secondary evaluation criteria:</u>** All the variables will be described using adapted statistics according to their type (quantitative data or qualitative data). For quantitative data a Wilcoxon or paired t test will be applied to assess the change from baseline and to compare the products.

	For qualitative data a McNemar's test will be applied to compare the proportion of improvement or satisfaction between the products. The bilateral approach will be used with a significance level of 0.05.
Foreseen study duration:	Clinical investigation beginning: Q1 2022 Clinical investigation end: Q2 2024 Clinical investigation global duration: 28 months Duration by subject: 24 months + screening period

FLOW-CHART

Procedure	**Visit 1 Screening**	**Visit 2 Day 0**	**Visit 3 M1[1/2]**	**Visit 4 M3**	**Visit 5 M6**	**Visit 6 M9**	**Visit 7 M12**	**Visit 8 M18**	**Visit 9 M24**
Days	D-x	D0	D40 ±2	D90 ±2	D180 ±4	D270 ±4	D365 ±7	D540 ±14	D730 ±14
Informed consent form signature	●								
Medical examination	●								
Medical history and previous and concomitant treatments collection	●								
Checking of the inclusion and exclusion criteria	●								
Pregnancy test		●[b]							
Confirmation of eligibility		●[b]							
Randomization		●							
WSRS live assessment by a blinded evaluator	●	●[b]	●[b]	●	●	●	●	●	●
Macrophotographs		●[b]	●[b]	●	●	●	●	●	●
Fringe projection acquisitions (2 areas)		●[b]	●[b]	●	●	●	●	●	●
Injection + anaesthesia (if necessary)		●	● Touch up						
GAIS live assessment by a blinded evaluator			●[b]	●	●	●	●	●	●
GAIS assessment by the subjects			●[b]	●	●	●	●	●	●
Subjective evaluation questionnaire for subjects			●[b]	●	●	●	●	●	●
ISR assessor		●[a]	●[b + a]	●	●	●	●	●	●
ISR subjects		completed each day during 4 weeks after injection and touch up if applicable at home by the subject							
Subjective evaluation questionnaire for injector		●[a]	●[a]						
AE and concomitant treatments and procedures collection	●	●	●	●	●	●	●	●	●
Study end									●

Keys:[b]: Before injection; [a]: After injection