Statistical Analysis Plan for the Study:

A first-in-human proof-of-concept study with NVDX3, an osteogenic implant of human allogenic origin, in the treatment of distal radius fractures in adults.

EUDRACT NUMBER: 2022-002304-21

CT number: 2023-508321-27-00

Version	Date	[redacted]	[redacted]	[redacted]
1.0	20 November 2024	[redacted]	[redacted]	[redacted]

For Approval:

[redacted]

[redacted]

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List of Abbreviations

AE	Adverse Event
AESI	Adverse Event of Special Interest
CI	Confidence Interval
CRF	Case Report Form
CSR	Clinical Study Report
CT	Computed Tomography
D	Day
DECT	Dual Energy Computed Tomography
DRF	Distal Radius Fractures
eLSS	extended Lane and Sandhu Scoring
ETV	Early Termination Visit
FU	Follow-Up
HD	Hospital Discharge
HIV	Human Immunodeficiency Virus
ICH	International Council for Harmonization
IMP	Investigational Medicinal Product
INN	International Nonproprietary Names
IS	Implant Surgery
M	Month
MedDRA	Medical Dictionary for Regulatory Activities
MMWS	Modified Mayo Wrist Score
NRS	Numeric Rating Scale
PoC	Proof-of-Concept
PT	Preferred Term
PRWE	Patient-Rated Wrist Evaluation
rAESI	Reportable Adverse Event of Special Interest
SAE	Serious Adverse Event
SAF	Safety Set
SAP	Statistical Analysis Plan
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
V	Visit
W	Week

1 Introduction

The purpose of the present Statistical Analysis Plan (SAP) is to precisely define the statistical analysis of the data of the study NVDX3-CLN01 (EudraCT number 2022-002304-21/CT number: 2023-508321-27-00). This SAP will cover the analysis of the primary and secondary endpoints. [redacted]

The SAP is based on the study protocol, version 6.0 (dated 25 June 2023) and the annotated CRF, version 5.0 (dated 21 March 2024). The SAP is prepared in compliance with ICH E9.

Any changes to the planned analyses occurring after finalization of the SAP will be described and justified in the Clinical Study Report (CSR).

1.1 Study Design

This study is a prospective, single arm, monocentric first-in-human Proof of Concept study in adult patients, suffering from a distal radius fracture, treated during the surgical intervention with NVDX3, an osteogenic implant from human allogeneic origin.

A patient is considered evaluable once he/she underwent the implant surgery with NVDX3.

As per standard of care, patients with DRF are followed up to 3 months post-intervention. In the context of this trial, patient safety and IMP efficacy will be followed up to 12 months post-implant surgery.

At the end of this study, the included patients will be invited to participate in a long-term safety follow-up study for an additional period of 10 years.

The study consists of the following phases:

- Screening (V1)
- Acute Safety FU
    - Implant Surgery - IS (V2)
    - Hospital Discharge - HD (V3)
    - Visit 4 (W2)
    - Visit 5 (W6)
- Mid-term[1] Safety FU
    - Visit 6 (M3)
    - Visit 7 (M6)
    - Visit 8 (M12)

1.2 Objectives of the Study

1.2.1 Primary Objective

The primary objective of this PoC study is to assess the safety of the NVDX3 implant.

1.2.2 Secondary Objective

The secondary objectives of this study are the following:

- To assess the acute and mid-term[1] safety of the NVDX3 implant.
- To assess the efficacy of the NVDX3 implant radiologically and clinically

1.2.3 Exploratory Objective

[redacted]

[1] "Mid-term follow-up" will replace "long-term follow-up" in the core study NVDX3-CLN01 to differentiate this time period from that of the long-term follow-up study, NVDX3-CLN0X, as detailed in Section 3.6.

1.3 Study Endpoints

1.3.1 Primary Endpoint

The primary endpoint is the evaluation of all SAEs and NVDX3 related AEs between screening (V1) and 12 months post-IS (V8).

1.3.2 Secondary Endpoints

1.3.2.1 Safety

- Description of all acute SAEs and NVDX3 related AEs between screening (V1) and 6 weeks post-IS (V5).
- Description of all Serious TEAEs and NVDX3 related TEAEs beyond 6 weeks (V5 excluded) until 12 months post-IS.
- Description of Treatment Emergent AEs (TEAEs) for the periods:
  - Between IS[2] and week 6 (V5 included)
  - Between week 6 (V5 excluded) till month 12 (V8 included)
  - Full study duration
- Description of related and unexpected AEs between inclusion* and study completion (TEAEs).
- Description of related and unexpected Serious AEs between inclusion* and study completion (serious TEAEs).
- Description of AEs of Special Interest between inclusion* and study completion (TEAESIs).
- Description of lab data and vital signs obtained between inclusion* and study completion.

*Inclusion refers to Implant Surgery, i.e. when the NVDX3 was implanted.

1.3.2.2 Efficacy

Radiological assessments on Computed Tomography data (CT) using the extended Lane and Sandhu Scoring tool (eLSS)

The following assessments will be performed at 3 and 12 months post-IS.

- Evaluation of bone formation status
- Evaluation of bone union status
- Evaluation of bone remodeling status
- Evaluation of Total extended Lane and Sandhu Score

Assessments will be compared to HD.

Radiological assessments on X-ray Using the eLSS tool

The following assessments will be performed at 2 and 6 weeks and at 3, 6 and 12 months post-IS according to standard of care.

- Evaluation of bone formation status
- Evaluation of bone union status
- Evaluation of bone remodeling status
- Evaluation of Total extended Lane and Sandhu Score

Assessments will be compared to HD[3].

[2] The assessment period for the acute events has been changed compared to the protocol, as detailed in Section 3.6.

[3] The baseline timepoint has been changed compared to the protocol, as detailed in Section 3.6.

Clinical assessments

The following assessments will be performed at HD, at 2 and 6 weeks and at 3, 6, and 12 months post-IS:

- Grip strength measure with a hydraulic hand dynamometer
- Modified Mayo Wrist Score (MMWS): A physician-based scoring evaluating the patients' pain, active flexion/extension arc, grip strength and ability to return to regular employment or activities.
- PRWE Questionnaire: A patient reported scoring evaluating the patients' wrist pain and disability.

The post-HD assessments will be compared to HD.

Numeric Rating Scale (NRS) for pain, a patient reported scoring evaluating the patients' pain, will be performed at screening, at HD and 2 and 6 weeks, 3, 6, and 12 months post-IS.
The post-screening assessments will be compared to screening.

1.3.3 Exploratory Endpoints

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

1.4 Sample Size Justification

No formal sample size calculation has been performed for this study since no formal hypothesis will have to be tested. However, as this is an early phase Proof of Concept study, the number of patients was limited to 10 individuals.

2 Data Considered for the Analysis

2.1 Patient Characteristics

At screening the following information is collected:

2.1.1 Demographic Data

-

2.1.2 Contraception Data

-

2.1.3 Smoking History

-

2.1.4 Employment Data

-

2.1.5 Index Fracture Classification

2.1.6 Medical History

-

[redacted]

2.2 Study Treatment Data

2.2.1 *Implant Surgery*

- [redacted]

If 'Yes',

2.2.2 *Drug Accountability*

- [redacted]

2.3 Efficacy

2.3.1 *Central Review CT using eLSS*

[redacted]

2.3.2 Central Review X-Ray

2.3.2.1 Efficacy assessment using eLSS:

[redacted]

2.3.2.2 Peri-operative measurements

[redacted]

[4] The baseline timepoint has been changed compared to the protocol, as detailed in Section 3.6.

2.3.3 Clinical Assessments

2.3.3.1 Grip Strength Test

[redacted]

2.3.3.2 Physician reported Modified Mayo Wrist Score

[redacted]

2.3.3.3 Patient reported Numerical Rating Scale for Pain

[redacted]

2.3.3.4 Patient-Rated Wrist Evaluation

[redacted]

-

2.4 Safety

2.4.1 *Adverse Events*

Information on adverse events will be collected throughout the study.

. If 'Yes':

Adverse events are coded

Any medical condition that is present at the time of the patient's screening will be considered as Medical History and not reported as an AE.

[redacted]

2.4.1.1 Acute Adverse Events

An acute adverse event is defined as an event that starts on or after the Implant Surgery (V2) till 6 weeks post-IS (V5 included).

2.4.1.2 Mid-term Adverse Events

A mid-term adverse event is defined as an event that starts after 6 weeks post-IS (V5 excluded) till study completion (completion V8 or early termination whichever comes first).

2.4.1.3 Treatment-emergent adverse events (TEAEs)

A Treatment-emergent adverse event (TEAE) is defined as an event that emerges after the NVDX3 was implanted, having been absent pre-implant surgery, or worsens relative to the preimplant state.

In case an event starts at the date of the surgery it will be decided at the DRM if the event can be considered as prior or treatment emergent based on input from the sites.

In case of a partial or missing date for the start of an adverse event it will be assumed that the event was treatment-emergent unless it can be determined from the partial start or stop date that the event definitely started before the NVDX3 was implanted.

2.4.1.4 Related Adverse Events

For each type of causality (NVDX3, grafting surgery, other study procedure) an adverse event is considered related if it is assessed as possibly, probably or definitely related or if the assessment is missing.

An adverse event will be considered NVDX3-related only in case the causality is NVDX3. It is not NVDX3-related if the cause is the grafting surgery or other study procedure.

2.4.1.5 Adverse Events of Special Interest (AESI)

The following adverse events will be considered as of special interest:

- Hypersensitivity reaction
- Immunological reaction
- An AE requiring immunosuppressive medication
- Ectopic bone formation
- Tumor formation
- Continued non-union/Non-fusion
- Refracture of the targeted area
- Revision surgery/intervention including removal of NVD-X3
- Any other condition considered by the treating physician as treatment failure

A reportable AESI (rAESI) is defined as an AESI that is assessed by the Principal Investigator as possibly, probably or definitely related to NVDX3.

2.4.1.6 Expectedness of Adverse Events

Each AE is assessed as expected or unexpected, in the light of the reference safety information (RSI) included in the latest version of the approved Investigator Brochure.

2.4.2 Safety Assessment by Local Radiologist

[redacted]

2.4.3 Laboratory Data

At Screening, HD, at 2 and 6 weeks and at 3, 6 and 12 months post-IS the following information is collected (at 3, 6 and 12 months post-IS: only upon occurrence or any suspicion of safety related issues):

2.4.3.1 Biochemistry

- [redacted]

2.4.3.2 Hematology

- [redacted]

2.4.3.3 Coagulation

- [redacted]

2.4.3.4 Serology (only at Screening)

- [redacted]

2.4.4 Vital Signs

At Screening, IS, HD, at 2 and 6 weeks and at 3, 6 and 12 months post-IS the following information is collected:

- Height (cm) (only at screening)
- Weight (kg)
- BMI (kg/m^2)
- Body temperature (°C)
- Pulse rate (beats/min)
- Respiratory rate (breaths/min)
- Mean systolic blood pressure (mmHg)
- Mean diastolic blood pressure (mmHg)

2.4.5 Physical Examination

At Screening, IS, HD, at 2 and 6 weeks and at 3, 6 and 12 months post-IS the following information is collected:

- [redacted]

- [redacted]

2.4.6 *Triplicate 12-Lead ECG*

At IS and at 12 months post-IS the following information is collected:

- [redacted]

2.4.7 *Pregnancy Test*

At Screening and at 12 months post-IS the following information is collected:

- [redacted]

2.5 Concomitant Treatments

2.5.1 *Concomitant Medications*

The following information on concomitant medications is collected:

- [redacted]

Concomitant medications will be coded [redacted]

2.5.2 *Concomitant Therapy*

The following information on concomitant therapies is collected:

- [redacted]

2.6 Course of the Study

2.6.1 *Study Dates*

- Date of written informed consent
- Date of each visit

2.6.2 *End of Study*

- [redacted]
- Date of study termination

- Primary reason for premature discontinuation (Withdrawal by patient, Adverse event, Protocol deviation, Study terminated by sponsor, Lost to follow-up, Death, Physician decision, Screen failure, Other), when applicable
- Date of death, when applicable

[redacted]

3 Statistical Methodology

3.1 Statistical Software

The SAS Version 9.4 statistical software package will be used for all statistical analyses.

3.2 Analysis Sets

The following analysis sets will be considered for the analysis:

Safety Set (SAF)

All patients treated with NVDX3.

Modified Full Analysis Set (mFAS)

All patients satisfying all inclusion criteria and none of the exclusion criteria and for whom any efficacy assessment is available.

The analysis sets will be determined by a review of the data prior to database lock.

The analysis of the demographic data and other baseline characteristics will be performed for both the SAF and the mFAS.

The analysis of efficacy will be performed on the mFAS.

The analysis of safety and concomitant treatments will be performed on the SAF.

3.3 Missing Data

No imputation strategies will be applied unless specified otherwise.

3.4 Summary Statistics

Unless specified otherwise, the following summary statistics will be used to describe the data:

- For quantitative variables: mean, 95% confidence interval (CI) on the mean, standard deviation (SD), minimum, 1st quartile, median, 3rd quartile, range, maximum, number of available and number of missing observations.
- For categorical variables: number and percentage for each of the scores or categories, and the number of observations.

3.5 Definition of Baseline

For the statistical analysis of change versus baseline for the efficacy endpoints the baseline is defined as the data collected at hospital discharge (HD)[5] except for the Numerical Rating Scale for pain where the observation at the screening visit will be used as the baseline.

[5] The baseline timepoint for radiological assessment on X-ray has been changed compared to the protocol, as detailed in Section 3.6.

3.6 Changes with Respect to the Analysis Foreseen in the Protocol

- With respect to the statistical analysis of adverse events the table showing frequency distributions and total number of events for patients with any SAE by MedDRA SOC and by MedDRA SOC and PT, and maximal severity will not be provided.
- For safety assessment, TEAEs will be described after the implant surgery, as per definition of treatment-emergent AEs. The assessment period between screening and week 6 post-IS (V5 included) indicated in the protocol for the acute events was erroneous and will be replaced by the assessment period between IS and week 6 post-IS (V5 included).
- For physical examination, the following additional data is recorded with respect to skin inspection of the affected arm:
    - Scar (Normal, Abnormal)
    - Open wound (Absent, Present)
    - Ulceration (Absent, Present)
    - Injury median nerve (Absent, Present)
- With respect to the radiological assessment on X-ray based on the eLSS tool the protocol mentions peri-operative X-ray acquisition as the baseline. However, instead of X-ray, fluoroscopic images were taken during surgery, which could not be used as baseline, because there was not guaranteed standardization regarding positioning and magnification. As a solution the X-ray acquired at Hospital Discharge (HD) is used as baseline for the eLSS assessments. It is confirmed by the principal central radiologist that this change does not impact the bone fusion scoring, as the image is acquired in the immediate post-operative period within days from surgery and considering the fact that bone fusion typically takes weeks to begin to be visualized by medical imaging. Furthermore, the protocol foresaw a central review of both CT and X-ray at Hospital Discharge (HD) but these assessments were not done since it is assumed that eLSS = 0 at baseline. As a consequence eLSS values were considered 0 at baseline defined as HD.
- Peri-operative measurements allowed to be performed on X-ray images acquired at hospital discharge, when quality fluoroscopy not sufficient.
- “Mid-term follow-up” will replace “long-term follow-up” in the core study NVDX3-CLN01 to differentiate this time period from that of the long-term follow-up study, NVDX3-CLN0X.

4 Details of the statistical analysis

4.1 Patient Characteristics

Summary statistics for demographic data and other baseline characteristics will be provided for the SAF and the mFAS.

4.1.1 Demographic Data

Descriptive statistics will be provided for:

- Approximate age at screening (years)

Frequency distributions will be provided for:

- Sex
- Race
- Childbearing potential status

4.1.2 Contraception Data

These data will be listed only

4.1.3 Smoking History

Frequency distributions will be provided for:

- Has the patient ever used tobacco?

Descriptive statistics will be provided for:

- Average daily cigarette count in the recent 12 months
- Duration of tobacco use (days)

4.1.4 Employment Data

These data will be listed only.

4.1.5 Index Fracture Classification

These data will be listed only.

4.1.6 Medical History

These data will be listed only.

4.2 Study Treatment

4.2.1 Implant Surgery

These data will be listed only.

4.2.2 Drug Accountability

Frequency distributions will be provided for estimated reconstituted volume used.

All other data will be listed only.

4.3 Efficacy Analysis

The analysis of all efficacy data will be performed on the mFAS.

4.3.1 Central radiological assessment of CT using eLSS

For the statistical analysis of eLSS data including bone formation, bone modeling and bone union as well as the eLSS total score, [redacted]

Frequency distributions will be provided at each scheduled visit for each of the following variables:

- Bone formation
- Bone remodeling
- Bone union

For the Total eLSS score descriptive statistics will be provided at each post HD visit.

Fequency distribution will be provided for the continued non-union at 12 months post-IS.

A profile plot will be provided for eLSS total score as well as a box plot showing eLSS total score at all post-IS visits.

A scatter plot presenting eLSS total score as assessed by the first reader versus second reader and a Bland-Altman plot will be created for the agreement between both readers. For both graphs, different symbols will be used for each visit on which the assessments are made.

Data from the both readers will be listed.

The following data will be listed only:

- Position and volume NVDX3
- Position and integrity of fixation devices
- Is the radius well aligned

4.3.2 Central radiological assessment of X-Ray using eLSS

For the statistical analysis of eLSS data including bone formation, bone modeling and bone union as well as the eLSS total score, [redacted]

Frequency distributions will be provided at each scheduled visit for each of the following variables:

- Bone formation
- Bone remodeling
- Bone union

For the Total eLSS score descriptive statistics will be provided at each post HD visit.

Fequency distribution will be provided for the continued non-union at 12 months post-IS.

A profile plot will be provided for eLSS total score as well as a box plot showing eLSS total score at all post-IS visits.

A scatter plot presenting eLSS total score as assessed by the first reader versus second reader and a Bland-Altman plot will be created for the agreement between both readers. For both graphs, different symbols will be used for each visit on which the assessments are made.

Data from the both readers will be listed.

The following data will be listed only:

- Position and volume NVDX3
- Position and integrity of fixation devices
- Is the radius well aligned

All peri-operative measurements will be listed only.

4.3.3 Clinical Assessments

4.3.3.1 Grip Strength Test

Descriptive statistics will be provided at each visit for the actual value and change versus baseline (HD) for the difference from normal.

The individual scores for each arm will be listed.

4.3.3.2 Physician reported Modified Mayo Wrist Score

Frequency distributions will be provided at each scheduled visit for each of the following variables:

- Pain
- Satisfaction
- Range of motion
- Grip Strength

Descriptive statistics will be provided at each visit for the total score.

Frequency distributions will be provided at each scheduled visit and shift tables between baseline (HD) and each post-baseline visit for the final result.

4.3.3.3 Numerical Rating Scale for Pain

Descriptive statistics will be provided at each visit for the actual value and change versus baseline (Screening) for the numerical rating scale for pain.

4.3.3.4 Patient-Rated Wrist Evaluation

Descriptive statistics will be provided at each visit for the actual value and change versus baseline (HD) for the following variables:

- Total pain score
- Total function score
- Total score

All subscores for pain and function will be listed.

4.4 Safety Analysis

The analysis of all safety data will be performed on the SAF.

4.4.1 Adverse Events

The analysis of adverse events will consist of:

- An overview of treatment-emergent adverse events consisting of:
  - Any TEAE
  - Any serious TEAE
  - Any NVDX3-related TEAE
  - Any NVDX3-related serious TEAE
  - Any TEAE related to the grafting surgery, including the applied medical device
  - Any TEAE related to other study procedure
  - Any unexpected TEAE
  - Any unexpected serious TEAE
  - Any severe TEAE
  - Any severe serious TEAE
  - Any treatment-emergent AESI
  - Any treatment-emergent rAESI
- Frequency distributions and total number of events for patients with any TEAE by MedDRA SOC and by MedDRA SOC and PT.
- Frequency distributions and total number of events for patients with any NVDX3-related TEAE by MedDRA SOC and by MedDRA SOC and PT.
- Frequency distributions and total number of events for patients with any TEAE by MedDRA SOC and by MedDRA SOC and PT, and maximal severity.

Frequency distributions will be provided for the entire study period (all treatment-emergent events), and broken down into IS till 6 weeks post-IS (V5 included) (acute events) and beyond 6 weeks post-IS (V5 excluded) till study completion (completion V8 or early termination whichever comes first) (mid-term).

Separate listings will be provided for:

- Non-Treatment-Emergent AEs
- Acute or Mid-term TEAEs
- Serious TEAEs
- TEAEs of special interest

4.4.2 Safety Assessment by Local Radiologist

These data will be listed.

4.4.3 Laboratory Data

These data will be listed only.

4.4.4 Vital Signs

Descriptive statistics at every scheduled visit will be provided for:

- Height (cm)
- Weight (kg)
- BMI (kg/m^2)
- Body temperature (°C)
- Pulse rate (beats/min)
- Respiratory rate (breaths/min)
- Mean systolic blood pressure (mmHg)

- Mean diastolic blood pressure (mmHg)

4.4.5 Physical Examination

These data will be listed.

4.4.6 Triplicate 12-Lead ECG

These data will be listed.

4.4.7 Pregnancy Test

These data will be listed.

4.5 Concomitant Treatments

4.5.1 Concomitant Medications

Medication that ends on the date of surgery will be considered as concomitant. Prior medication will only be these medications clearly stopping before the date of surgery.

A table will be provided showing frequency distributions of patients taking concomitant medication by anatomical class and therapeutic class for the SAF.

A listing will be provided for all medications.

A separate listing will be provided for pain medications.

In both listings it will be indicated whether the medication started before or after the start time of surgery.

[redacted]

4.5.2 Concomitant Therapy

These data will be listed.

4.6 Sample Description

4.6.1 Disposition of Patients

The following information will be provided:

- Number of patients in each analysis set and at each visit.
- Date of first and last inclusion visit (signing informed consent) and date of last sudy visit for each analysis set.
- Descriptive statistics for study duration.
- Frequency distributions of premature study discontinuation and its reason for each analysis set.

4.6.2 Protocol Deviations

A table will be provided showing frequency distributions of patients with major protocol deviations, total and broken down by type of deviation.

A listing will be provided of all protocol deviations.

5 Overview of Assessments

		Screening	Acute safety FU				Long-term safety FU			Early Termination
		V1	V2 [1]	V3	V4	V5	V6	V7	V8	ETV
					W2	W6	M3	M6	M12	
			Implant Surgery IS (Max 7 days after DRF diagnosis)	Hospital Discharge HD	IS+13d ± 2d	IS+42d ±7d	IS+90d ± 15d	IS+180d ± 30d	IS+360d ± 30d	
Informed consent		×							×[9]	×[9]
Eligibility criteria		×								
Demography		×								
Medical and concomitant medication history		×								
Index fracture evaluation/classification		×								
Physical examination		×	×	×	×	×	×	×	×	×
Weight/Height (BMI)[8]		×	×	×	×	×	×	×	×	×
Triplicate 12-Lead ECG			×						×	
Vital signs		×	×	×	×	×	×	×	×	×
Inspection of the skin of the affected arm[2]		×	×	×	×	×	×	×	×	×
Standard safety laboratory[3]		×		×	×	×	(×)	(×)	(×)	
Serology (HIV, HBV & HBC)		×								
Pregnancy test[4]		×							×	
Implant Surgery (IS)			×[5]							
Peri-operative IS related information			×							
Grip strength test				×	×	×	×	×	×	
NRS-pain		×		×	×	×	×	×	×	
PRWE				×	×	×	×	×	×	
MMWS				×	×	×	×	×	×	
Radiological efficacy[6]	AP/LAT X-ray	×*	×[7]*	×*	×*	×*	×*	x	×	
	DECT-scan	×* (Normal CT)		×			×		×	
AE/SAE collection			×	×	×	×	×	×	×	×
Concomitant medication			×	×	×	×	×	×	×	×
Concomitant therapy				×	×	×	×	×	×	×

1 In-clinic stay: The patient may be hospitalized before the surgery following to hospital standard of care. The required pre-operative assessments can be done up to 3 days before the surgery.
2 Skin inspection to evaluate potential surgical site infections.
3 At screening, Discharge, V4 and V5: safety laboratory analyses are mandatory. At V6, V7 and V8: Upon occurrence or any suspicion of safety related issues.
4 In women of childbearing potential only: a serum pregnancy test will be performed at Screening and at V8
5 Follow the instructions ad per "NVDX3 handling Manual".
6 To guarantee image quality, all X-rays and CT-scan acquisitions will need to strictly follow the imaging instructions as described per "Imaging Acquisition Manual".
7 AP/LAT X-rays: both after insertion of fixation device, and after insertion of the NVDX3 implant (at the end of the surgery)
8 Height at screening only
9 Informed consent proposing participation to the long-term safety follow-up study (NVDX3-CLN0X)
* Standard of care image acquisitions for the diagnosis and follow-up of DRF