Study Protocol

Efficacy of the BioWick® SureLock® Implant for the Reattachment of Soft Tissue to Bone in Subjects Undergoing Rotator Cuff Repairs

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CAYENNE MEDICAL, INC., A ZIMMER BIOMET COMPANY

CLINICAL RESEARCH PROTOCOL

Efficacy of the BioWick® SureLock® Implant for the Reattachment of Soft Tissue to Bone in Subjects Undergoing Rotator Cuff Repairs

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1. CONTACTS

Contact the following individuals for all other inquiries and information about this study:

Program Director	**Clinical Study Manager**
[REDACTED]	[REDACTED]

2. SPONSOR SIGNATURE

My signature, in conjunction with the signature of the investigator, confirms the agreement of both parties that the clinical study will be conducted in accordance with the protocol and applicable laws and other regulations including, but not limited to, the ICH Guideline for Good Clinical Practice, the US Code of Federal Regulations, protections for privacy, and generally accepted ethical principles for human research such as the Declaration of Helsinki.

Nothing in this document is intended to limit the authority of a physician to provide emergency medical care.

Sponsor Representative Signature	Date of Signature (DD MMM YYYY)

Sponsor Representative Name and Title (print)

3. INVESTIGATOR SIGNATURE

I have read this protocol and agree that it contains all necessary details to carry out the study as described. I will conduct this protocol as outlined herein, including all statements regarding confidentiality. I will make a reasonable effort to complete the study within the time designated. I will provide copies of the protocol and access to all information furnished by the Sponsor to study personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the test and the study. I understand that the study may be terminated or enrollment suspended at any time by the Sponsor, with or without cause, or by me if it becomes necessary to protect the interests of the study subjects. Any supplemental information that may be added to this document is also confidential and proprietary to Cayenne Medical, Inc., a Zimmer Biomet company, and must be kept in confidence in the same manner as the contents of this protocol.

I agree to conduct this study in full accordance with all applicable regulations and Good Clinical Practice.

Investigator's Signature	Date of Signature (DD MMM YYYY)
Investigator's Name (print)	

4. DISCLOSURE STATEMENT

4.1 Restricted Distribution of Documents

This document contains information that is confidential and proprietary to Cayenne Medical, Inc., a Zimmer Biomet company This information is being provided solely for the purpose of evaluating and/or conducting the clinical trial for Cayenne Medical, Inc. You may disclose the contents of this document only to study personnel under your supervision, IRBs, or authorized representatives of regulatory agencies for this purpose under the condition that they maintain confidentiality.

The contents of this document may not be used in any other clinical trial, disclosed to any other person or entity, and/or published without the prior written permission of the Sponsor. The foregoing shall not apply to disclosure required by any regulations; however, you will give prompt notice to Cayenne Medical, Inc. of any such disclosure.

All other nonpublic information provided by Cayenne Medical, Inc., as well as any information that may be added to this document, is also confidential and proprietary to Cayenne Medical, Inc. and must be kept in confidence in the same manner as the contents of this document.

5. LIST OF ABBREVIATIONS

Abbreviation	Term
AE	Adverse Event/Adverse Experience
CFR	Code of Federal Regulations
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
DMP	Data Management Plan
EDC	Electronic Data Capture
EMG-NCV	Electromyelopathy and Nerve Conduction Velocity
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
iCRF	Internet Case Report Form
IRB	Institutional Review Board
ITT	Intent to Treat
IV	Intravenous
MCS	Mental Component Score
PC	Personal Computer
PCS	Physical Component Score
PHI	Protected Health Information
PI	Principal Investigator
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SDV	Source Document Verification
SOC	Standard of Care
TEAE	Treatment Emergent Adverse Event
UHMWPE	Ultra High Molecular Weight Polyethylene
UPS	United Parcel Service
USA or U.S.	United States of America
USB	Universal Serial Bus
VAS	Visual Analog Scale
VR-12	Veterans RAND 12 Item Health Survey

6. SYNOPSIS

Study Title	Efficacy of the BioWick® SureLock® Implant for the Reattachment of Soft Tissue to Bone in Subjects Undergoing Rotator Cuff Repairs
Sponsor	Cayenne Medical, Inc., a Zimmer Biomet company
Study Design	The study is a prospective, non-randomized, open-label, single-arm study that includes both preoperative assessments and follow-up assessments at 3 months, 6 months, and 12 months.
Clinical Phase	Postmarket
Number of Sites	Up to ten sites in the U.S.
Study Duration per Subject	Subjects will be enrolled in the study for up to 12 months.
Primary Objective	The primary objective of this study is to assess survivorship (lack of reoperation/device removal) with the use of the BioWick SureLock implant.
Secondary Objective	The secondary objectives of this study are : • To document the postmarket effectiveness of the BioWick SureLock implant using range of motion measurements, ASES scores, VR-12 scores, and VAS scores, with the corresponding assessments made at 3 months, 6 months, and 12 months. • To document device safety via device-related adverse events reported over the course of the study.
Primary Endpoint	The primary endpoint of this study is the BioWick SureLock implant survivorship at 12 months post-operative.
Secondary Endpoints	The secondary endpoints of this study are: • Implant survivorship at visit intervals other than 12 months • VR-12 scores at 3 months, 6 months, and 12 months postoperative • ASES rating scale at 3 months, 6 months, and 12 months postoperative • VAS pain scores at 3 months, 6 months, and 12 months postoperative • Range of motion (ROM) at 3 months, 6 months, and 12 months postoperative

Inclusion Criteria	**Inclusion Criteria** 1. Clinical diagnosis of rotator cuff tear which is greater than or equal to 1.5 cm and less than or equal to 4.0 cm full thickness of either the supraspinatus or infraspinatus determined by MRI which has not been previously repaired; 2. Goutallier Stage 2 or less; 3. Patte Stage II (mid humeral head retraction); 4. Tear(s) confirmed intra-operatively by calibrated probe, tears measured in both anterior-posterior and medial-lateral planes; 5. Subject is skeletally mature at the surgical site; 6. Subject is able to read and understand the ICF and has voluntarily provided written informed consent.
Exclusion Criteria	1. Clinical diagnosis of a rotator cuff tear of the subscapularis that requires repair (not including debridement); 2. Conditions which, in the opinion of the Principal Investigator, may limit the subject's ability or willingness to follow post-operative care or study instructions; 3. If female, subject is pregnant; 4. Presence of local or systemic infection; 5. Suprascapular nerve compression requiring release or documented by EMG-NCV; 6. Substance abuse, including tobacco, alcohol, or illicit drugs which, in the investigator's judgment, could impair healing or influence study compliance; 7. Foreign body sensitivity. If material sensitivity is suspected, testing should be completed prior to device implantation; 8. Insufficient blood supply or previous infection which may hinder the healing process; 9. Subject conditions including: insufficient quantity or quality of bone or soft tissue, or immature bone where the device may impact or disrupt the growth plate; 10. Subject is a prisoner or member of another vulnerable population; 11. Cortisone injection within 6 weeks prior to surgical treatment; 12. Use of immune suppressants or chemotherapeutic medications within the last 12 months;

	13. Use of systemic corticosteroids at any daily dose for more than 1 month within the last 12 months.
Safety Evaluation	Safety evaluations will be based on the frequency and incidence of device related adverse events.
Planned Sample Size	A maximum of 71 subjects will be enrolled in the study.
Statistical Analysis	The following analysis populations will be defined for the study: **Intention to Treat (ITT) Population** – The ITT population will consist of all subjects who have signed informed consent, been enrolled in the study, and have had successful placement of the BioWick™ SureLock™ implant. **Safety Population** – The safety population will consist of all subjects who have signed informed consent, been enrolled in the study, and have had a procedure during which BioWick SureLock implant placement was attempted, whether or not placement was successful. The primary analysis population for all primary and secondary endpoints will be the ITT population. The primary analysis population for safety will be the safety population. **Analysis of Primary Endpoint** Implant survivorship for each subject will be determined by whether the subject undergoes a device removal/revision/reoperation of the study device.

7. SCHEDULE OF STUDY EVENTS

Table 7.1 Study Flowchart of Scheduled Events

Event	Screening (Day -28 to -1)	Enrollment/ Visit 1 (Day 1)[1]	3 Months/ Visit 2 (Day 90 ± 14 Days)	6 Months/ Visit 3 (Day 180 ± 30 Days)	12 Months/ Visit 4 Or Early Termination Visit[2] (Day 365 ± 30 Days)
Informed Consent	X				
Inclusion/Exclusion Criteria	X	X			
Medical History	X				
Physical Exam	X				
Concomitant Medications	X	X	X	X	X
BioWick SureLock Surgical Implantation		X			
Magnetic Resonance Imaging	X[3]				
ASES Rating Scale	X		X	X	X
VR-12 Health Survey	X		X	X	X
ASES Range of Motion	X		X	X	X
Adverse Events	X	X	X	X	X
Subject Completion					X

[1] Upon meeting all I/E criteria, subjects will be enrolled on Day 1 after final confirmation of intra-operative I/E criteria.
[2] Assessments to be completed if the subject is an early withdrawal and returns to the clinic for a final visit.
[3] A MRI scan obtained within 6 months of screening may be used to confirm I/E criteria. If a MRI scan is not available within this time frame, then a screening MRI scan is required.

8. ETHICAL CONSIDERATIONS

This clinical study is designed to comply with International Conference on Harmonization (ICH) Guidance on General Considerations for Clinical Trials (62 FR 66113, 17 Dec 1997), Clinical Investigation of Medical Devices for Human Subjects -- Good Clinical Practice (ISO14155:2011), and Good Clinical Practice: Consolidated Guidance (62 FR 25692,09 May 1997).

8.1 Institutional Review Board

It is the responsibility of the investigator to obtain the approval of the IRB before the start of the study. The IRB must be registered and active with the Office for Human Research Protections of the US Department of Health and Human Services. A copy of the approval letter along with a roster of IRB members and/or the US Department of Health and Human Services Federal Wide Assurance Number will be retained as part of the study records. During the course of the study, the investigator will provide timely and accurate reports to the IRB on the progress of the study at appropriate intervals (not to exceed 1 year) and at the completion of the study. The investigator will notify the IRB of SAEs, protocol deviations or other significant safety findings per IRB guidelines. The study protocol, ICF, advertisements (if any), and amendments (if any) will be approved by the IRB in conformance with CFR, Title 21, Part 56.

8.2 Ethical Conduct of the Study

The study will be conducted in full compliance with applicable FDA regulations and ICH guidelines for GCP and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

8.3 Subject Information and Consent

A copy of the proposed informed consent documents will be submitted to the Sponsor for review and approval before submission to the appropriate IRBs. The study will not begin until the documents have been reviewed and approved by the Sponsor and the documents have been approved by the IRBs.

The ICF shall contain all of the elements of informed consent specified in the Code of Federal Regulations (21 CFR 50.25) and HIPAA authorization. Copies of the regulations relating to informed consent and the protection of human subjects in clinical studies are available from the Sponsor.

All potential study subjects will be given copies of the following before participating in any screening procedures:

- The study ICF;
- Agreement for HIPAA Authorization (if separate from ICF);
- Any specific documentation that may be required by the site's IRB.

Subjects will have an opportunity to discuss the contents of these forms with study site staff. The study should be thoroughly explained including the purpose of the study, methods, anticipated benefits, and potential hazards prior to obtaining written consent.

Subjects must understand and voluntarily sign these forms in compliance with 21 CFR, Part 50, before participating in any study-related procedures. Subjects will be made aware that they may withdraw from the study at any time.

The subject will be made aware of his/her right to see and copy his/her records related to the study for as long as the investigator has possession of this information. If the subject withdraws consent and/or HIPAA authorization, the investigator can no longer disclose health information, unless it is needed to preserve the scientific integrity of the study. A copy of the signed informed consent document will be given to the subjects for their records.

The subjects will also be informed that their medical records may be reviewed by the study Sponsor or designee, quality assurance auditor, or inspector from FDA or similar foreign authorities. The subjects will be informed that these persons are bound by the same confidentiality obligations as the subject's physician.

Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care under applicable regulations. Regulations require that Investigators

permit the Sponsor, Sponsor representatives, and appropriate regulatory agencies to conduct inspections and review records pertaining to clinical investigations.

The delegation of Investigator responsibilities, including obtaining informed consent, must be documented in the study records.

8.4 Subject Confidentiality

The Principal Investigator and designees, employees, and agents involved with this study will comply with relevant state and federal laws relating to the confidentiality, privacy, and security of subject's PHI. They will only create, maintain, use, or disclose any data that is generated by this study or other information disclosed to the Principal Investigator or their employees or agents during the course of the study to the Sponsor, IRB, FDA, or other authorized recipients as appropriate for the execution, analysis, review, and reporting of this study. Such information shall not be used for any other purposes and will remain confidential.

Subject records are only to be identified by initials and subject ID numbers. Subject names are not to be transmitted on any document to the Sponsor.

9. INTRODUCTION

9.1 Background and Current Treatment

Fixation in soft tissues is traditionally achieved by using a solid anchor which has been loaded with non-absorbable sutures, a technique which has proven adequately effective but which carries the risk of displacement or relocation of the anchor as well as bone loss and/or articular damage. Additionally, existing products require manual "tugging" of the anchor in order to achieve deployment, and, in the event that the anchor is not deployed correctly, the anchor may subsequently pull out.

9.2 BioWick SureLock Implant

The BioWick SureLock implant is a device for shoulder and extremity surgery, constructed of Ultra High Molecular Weight Polyethylene Suture. BioWick SureLock is uniquely designed to minimize these risks by avoiding manual tensioning with an inserter mechanism that ensures that the implant is consistently deployed below the cortex.

9.3 Rationale for This Study

The purpose of this study is to collect postmarket data in subjects who receive surgical treatment of a full-thickness rotator cuff tear (of at least 1.5 cm) with the BioWick SureLock implant. Both performance and safety data will be collected.

10. OBJECTIVES

10.1 Primary Objective

The primary objective of this study is to assess survivorship (lack of reoperation/device removal) with the use of the BioWick SureLock implant.

10.2 Secondary Objectives

The secondary objectives of this study are:

- To document the postmarket effectiveness of the BioWick SureLock implant using ASES scores, VR-12 scores, and VAS scores, with the corresponding assessments made at 3 months, 6 months, and 12 months postoperative.
- To document the postmarket effectiveness of the BioWick SureLock implant using range of motion (ROM) measurements with the corresponding assessments made at 3 months and 6 months postoperative.
- To document device safety via device-related adverse events reported over the course of the study.

11. STUDY DESIGN

The study is a prospective, non-randomized, open-label, single-arm, postmarket, multicenter study. The schedule of study events list the procedures to be performed in each visit (see Table 7.1).

11.1 Measures Taken to Avoid Bias

11.1.1 Randomization

All subjects enrolled in the study will be treated with the BioWick SureLock implant. As there is no comparison arm, there will be no randomization.

11.1.2 Blinding

As this study is a single-arm study in which all subjects are treated with the BioWick SureLock implant, neither subjects nor investigators will be blinded.

11.1.3 Description of the Study Device

The BioWick SureLock implant is a device constructed of ultra-high molecular weight polyethylene suture for use in shoulder and extremity surgery. The BioWick SureLock implant eliminates manual tensioning through a unique inserter-controlled deployment method that prevents partial deployment as well as displacement or partial deployment of the anchor by consistent deployment of the anchor below the cortex. The inserter is made of surgical grade stainless steel and plastic, and the wick component is made of 85/15 PLGA (L-lactide-coglucolide).

12. SELECTION OF STUDY POPULATION

Subjects will be recruited from patients requiring rotator cuff repair surgery or have previously had a rotator cuff tear repaired using the BioWick SureLock implant.

12.1 Inclusion Criteria

Subjects must meet all of the following inclusion criteria to participate in this study:

Inclusion Criteria

1. Clinical diagnosis of rotator cuff tear which is greater than or equal to 1.5 cm and less than or equal to 4.0 cm full thickness of either the supraspinatus or infraspinatus determined by MRI, which has not been previously repaired;
2. Goutallier Stage 2 or less;
3. Patte Stage II (mid humeral head retraction);
4. Tear(s) confirmed intra-operatively by calibrated probe, tears measured in both anterior-posterior and medial-lateral planes;
5. Subject is skeletally mature at the surgical site;
6. Subject is able to read and understand the ICF and has voluntarily provided written informed consent.

12.2 Exclusion Criteria

Any subject who meets any of the exclusion criteria will be excluded from participation in this study:

1. Clinical diagnosis of a rotator cuff tear of the subscapularis that requires repair (not including debridement);
2. Conditions which, in the opinion of the Principal Investigator, may limit the subject's ability or willingness to follow post-operative care or study instructions;
3. If female, subject is pregnant;
4. Presence of local or systemic infection;
5. Suprascapular nerve compression requiring release or documented by EMG-NCV;
6. Substance abuse, including tobacco, alcohol, or illicit drugs which, in the investigator's judgment, could impair healing or influence study compliance;
7. Foreign body sensitivity. If material sensitivity is suspected, testing should be completed prior to device implantation;
8. Insufficient blood supply or previous infection which may hinder the healing process;
9. Subject conditions including: insufficient quantity or quality of bone or soft tissue, or immature bone where the device may impact or disrupt the growth plate;
10. Subject is a prisoner or member of another vulnerable population;
11. Cortisone injection within 6 weeks prior to surgical treatment;
12. Use of immune suppressants or chemotherapeutic medications within the last 12 months;

13. Use of systemic corticosteroids at any daily dose for more than 1 month within the last twelve months.

12.3 Subject Withdrawal

Subjects may discontinue from the study at any time. A subject may be discontinued from the study for the following medical or administrative reasons:

- **Subject Withdrawal of Consent -** Subjects will be free to discontinue from the study at any time and for any reason but must notify the study site of their exit from the study.
- **Adverse Event –** If during the procedures the subject suffers an AE that, in the judgment of the PI, Sponsor or medical monitor, presents an unacceptable consequence or risk to the subject, the subject will be discontinued from further participation in the study.
- **Lost to Follow Up –** Subjects discontinue from the study without notifying the study site.
- **Serious Protocol Violation –** If, during enrollment in the study, the subject fails to follow, violates or refuses to participate in any of the procedures described in the protocol then the subject will be discontinued from the study at the discretion of the Sponsor. If, at any point during the study, a subject is determined to have been erroneously enrolled into the study, the subject will be discontinued from the study due to protocol violation.
- **Other -** If the above reasons are not applicable, "Other" will be selected as the option and the appropriate reason for subject withdrawal provided.

For subjects who discontinue or are withdrawn from the study for any reason, the PI will notify the Sponsor and attempt to recover the following:

- AE occurrences since the last visit to the study site
- Concomitant medication usage since the last visit to the study site

If the subject is withdrawn at a study visit, the procedures for an early termination visit will be conducted to assess their continued well-being.

13. STUDY PROCEDURES

13.1 Subject Identification

Each subject will be assigned a unique subject number. Subject numbers will not be reassigned or reused for any reason. Only their assigned subject number, initials, and date of birth should identify subjects to the Sponsor. The investigator must maintain a list of potential subjects and enrolled subjects using the Subject Screening/Enrollment Log.

Any potential subjects who are pre-screened can be added to the log by recording their screening number and initials only. Those who sign the ICF will be assigned a unique study ID.

13.2 Subject Enrollment

Subjects who meet all inclusion and exclusion criteria will be considered eligible for enrollment. Subjects will be considered enrolled on Day 1 following final confirmation of the intra-operative inclusion/exclusion criteria. Hence, subjects who begin a surgical procedure may exit the study as a screen failure. Once enrolled, a subject may only exit the study as a withdrawal (not a screen failure). The reason for withdrawal will be documented by the investigator on the Subject Screening/Enrollment Log.

13.3 Screen Failures

Subjects who sign an informed consent form and fail to meet the inclusion and/or exclusion criteria are defined as screen failures. For all screen failures, the investigator will record the reason for the screen failure on the Subject Screening/Enrollment Log. A copy of the log will be retained in the investigator's study files.

13.4 Description of Study Procedures

Subjects enrolled will follow the study procedures outlined in Section 13.

13.4.1 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of the rotator cuff tear will be obtained during screening (baseline). A screening MRI scan will not be required if a MRI scan was obtained within 6 months of screening based on a review of the subject's medical history. All pre-operative screening or prior qualifying scans and post-operative study scans should be performed on a 1.5T magnet or better. Additionally, a standardized imaging protocol will be utilized for all images collected as part of the study procedures.

All radiographic images will be read and reviewed by Medical Metrics Inc. to confirm inclusion criteria.

13.4.2 Veterans RAND 12-Item Health Survey (VR-12)

The VR-12 is a 12-item self-administered health survey. The VR-12 consists of eight scales which evaluate physical health and mental health.

Physical Health Scales:
- General Health
- Physical Functioning
- Role-Physical
- Bodily Pain

Mental Health Scales:
- Role-Emotional

- Vitality
- Mental Health
- Social Functioning

The responses to the physical health scales will be evaluated to produce the Physical Component Score (PCS), and the responses to the mental health scales will be evaluated to produce the Mental Component Score (MCS). Both the PCS and MCS will be determined for all subjects at screening, and at 3 months, 6 months, and 12 months postoperative.

13.4.3 ASES Rating Scale

The American Shoulder and Elbow Surgeons (ASES) Functional Questionnaire is an eleven-item self-report questionnaire consisting of ten questions which evaluate function and one question that evaluates pain. The function section of the survey yields a score between 0 and 30, with a score of zero indicating maximum disability. VAS Pain Score is included and is measured on a ten point scale, with a maximum pain score of ten. ASES Ratings will be determined for all subjects at screening, and at 3 months, 6 months, and 12 months postoperative.

13.4.4 Delivery of BioWick SureLock Implant

The approved surgical technique will be followed for delivery of the BioWick SureLock Implant. The surgical technique will be provided separately.

13.5 Procedures To Be Conducted at Each Study Site Visit

13.5.1 Screening (Day -28 to -1)

The screening period of the study will take place up to 28 days prior to enrollment. Subjects will visit the study site and receive initial study documents including the ICF. Subjects will be given ample time to review and ask any questions about the clinical trial prior to signing informed consent. Once informed consent is obtained, the subject will be screened according to inclusion and exclusion criteria.

Site personnel will evaluate the subject's current pain level using the VAS pain scale. Disability and function will be assessed through evaluation of ASES scores, VR-12 scores, and ROM measurements. These evaluations will serve as the preoperative baseline scores.

Screening Visit Tasks

- Informed consent
- Inclusion/exclusion criteria
- Assess prior medications
- Medical history
- Physical exam

- MRI exam (may be obtained from medical history within previous 6 months)
- ASES Physician and Patient Scores
- VR-12 scores
- Concomitant Medications

13.5.2 Enrollment/Visit 1 (Day 1)

Subjects who meet all pre-operative inclusion/exclusion criteria will return to the study site for their surgical procedure and enrollment into the study. Upon arrival at the site and final confirmation of the pre-operative inclusion/exclusion criteria, the subject will be prepped for the surgical procedure. Final confirmation of the inclusion/exclusion criteria will be made intra-operatively, at which point subjects will be enrolled in the study if they continue to be study-eligible.

Standard post-operative care will occur for all subjects according to site procedures. The subjects will be assessed for any adverse events that have occurred following the placement of the study device and concomitant medications will be recorded. Prior to hospital discharge, the site will go over all rehabilitation procedures with the subject per the rehabilitation protocol for the study.

Enrollment/Visit 1 Tasks

- Confirm pre-operative inclusion/exclusion criteria
- Surgical Procedure
    - Confirm intra-operative inclusion/exclusion criteria
    - Use of BioWick SureLock implant
- Assess any AEs

13.5.3 3 Months/Visit 2 (Day 90 ± 14 Days)

Upon arrival at the clinic, site personnel will evaluate the subject's current pain level using the ASES. Disability and function will be assessed through evaluation of ASES scores and VR-12 Scores. The subject will be asked about any adverse health events that have occurred since implantation of the device as well as any medications they are taking.

Visit 2 Tasks

- VAS scores
- ASES scores
- VR-12 scores
- ROM measurements
- Assess AEs
- Concomitant medications

13.5.4 6 Months/Visit 3 (Day 180 ± 30 Days)

Upon arrival at the clinic, site personnel will evaluate the subject's current pain level using the ASES. Disability and function will be assessed through evaluation of ASES scores, and VR-12 Scores. The subject will be asked about any adverse health events that have occurred since the last study visit as well as any medications they are taking.

Visit 3 Tasks

- VAS scores
- ASES scores
- VR-12 scores
- ROM measurements
- Assess AEs
- Concomitant medications

13.5.5 12 Months/Visit 4 (Day 365 ± 30 Days)

Upon arrival at the clinic, site personnel will evaluate the subject's current pain level using the ASES. Disability and function will be assessed through evaluation of ASES scores, and VR-12 Scores. The subject will be asked about any adverse health events that have occurred since implantation of the device as well as any medications they are taking.

Visit 4 Tasks

- VAS scores
- ASES scores
- VR-12 scores
- ROM measurements
- Assess AEs
- Concomitant medications
- Complete Study Completion CRF

After completion of the final procedure required for this visit, the subject's participation in the study is complete, and the site should fill out the Study Completion Case Report Form (CRF).

13.5.6 Coronavirus (COVID-19) Expectations

If subjects are not allowed at the clinic for visits or if subjects refuse to come into the clinic due to COVID-19, then the following tasks should take place:

- Subject questionnaires (VAS, ASES, and VR-12) will be mailed to the subject for completion. These questionnaires should not be completed via phone. If the site does not receive a response from the subject, the site must attempt to contact the subject

and/or re-mail the subject questionnaires at least three (3) times within the visit window before submitting a protocol deviation, unless a response is received.

- The site will attempt to contact the subject to inquire of adverse events that may have occurred and/or been resolved since their last visit. The site is required to perform at least three (3) contact attempts to obtain this information. These contact attempts must be documented in the subject's study binder. If there is no response by the end of the visit window, a note-to-file (NTF) must be added to the subject's study binder indicating new adverse events were not confirmed for the visit.
- ROM measurements will not be required; however, a protocol deviation must be submitted.
- Label protocol deviations as being related to COVID-19, as applicable

Please note that these expectations are *specifically* for COVID-19 situations. If a subject misses a visit unrelated to COVID-19, this section does not apply and a "Missed Visit" protocol deviation will be submitted.

14. SAFETY

14.1 Safety Variables

Safety will primarily be assessed through frequency and incidence of adverse events..

15. EFFECTIVENESS

15.1 Effectiveness Variables

15.1.1 Primary

The primary endpoint of this study is survivorship (lack of reoperation/device removal) at 12 months postoperative.

15.1.2 Secondary

The secondary endpoints of this study are:

- Implant survivorship at visit intervals other than 12 months
- VR-12 scores at 3 months, 6 months, and 12 months postoperative
- ASES rating scale at 3 months, 6 months, and 12 months postoperative
- VAS pain scores at 3 months, 6 months, and 12 months postoperative
- Range of motion (ROM) at 3 months, 6 months, and 12 months postoperative

The above endpoints based on continuous data will be reported as both raw and change from baseline (CFB) results.

16. STATISTICAL ANALYSIS AND PLANNED ANALYSIS

16.1 Introduction

This study is a post-marketing, single treatment group, prospective study conducted at up to three study centers. The study will be conducted at as many as ten (10) centers in the U.S. Subjects will be enrolled in the trial for a period of 12 months. The objectives of the statistical analyses are to evaluate safety and effectiveness of the BioWick SureLock implant in the reattachment of soft tissue to bone in rotator cuff repairs.

A study center is defined as a hospital or medical office under the control and supervision of the Principal Investigator.

16.2 Sample Size and Power

The study is sized with respect to the primary one-year survivorship endpoint of the study. Assuming an observed one-year survivorship of 85%, a total of 59 subjects is required in order to estimate the true survivorship within a 95% confidence interval with a half-width precision of 10.7%. This assumes a two-sided α=0.05 level of significance and that the data come from a binomial distribution. In order to account for a 15% lost-to-follow-up rate, the sample size will be upwardly adjusted to 71 total subjects.

16.3 Analysis Populations

The following analysis populations will be defined for the study:

ITT Population – The ITT population will consist of all subjects who have signed informed consent, been enrolled in the study, and have had a successful placement of the BioWick SureLock implant.

Safety Population – The safety population will consist of all subjects who have signed informed consent, been rolled in the study and have had a procedure during which placement of the BioWick SureLock implant was attempted, whether or not placement was successful.

The primary analysis population for all primary and secondary endpoints will be the ITT population. The primary analysis population for safety will be the safety population.

16.4 Analysis Subgroups

Analysis subgroups may include age group.

16.5 Statistical and Analytical Plans

16.5.1 Primary Endpoint Analyses

Implant survivorship for each subject will be determined by whether the subject undergoes a revision or reoperation of the study device. Survivorship will be assessed using a Kaplan-

Meier analysis. Data will be considered right-censored for all patients that do not have a device failure. For patients lost-to-follow-up, their last available clinical visit will be used as the censored date. For patients that die during the study, their death date will be used as the censored date. The survivorship point estimate and 95% confidence interval about the point estimate will be calculated for the one-year primary endpoint.

16.5.2 Secondary Endpoint Analyses

Summary statistics (mean, standard deviation, sample size, median, minimum, and maximum) will be computed for all quantitative secondary effectiveness endpoints on the raw and change from baseline data by time point. Frequency counts and percentages will be reported for all categorical secondary effectiveness endpoints.

16.6 Handling Missing Data

In the statistical analysis of the primary effectiveness endpoint of the study, only subjects with evaluable endpoint will be used in the statistical analysis, i.e., a complete case analysis.

16.7 Interim Analysis

Interim analysis can be performed at any point during the duration of the study.

17. ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

Equipment, supplies, and properly skilled personnel must be available to treat any unexpected reaction.

17.1 Safety

Although major AEs are not anticipated, the investigator must proceed with utmost caution.

The AEs reported will be evaluated as to incidence, relationship to the time the device was used, how long the device had been in use, severity, and relationship to the medical device.

The section on AEs will be tabulated by severity and by Investigator's assessment of the event's causative relation to treatment. AE counts by severity level (mild, moderate, and severe) will be tabulated.

17.2 Definitions

The term "adverse event," as used by the Sponsor, is synonymous with the term "adverse experience," which is used by the FDA.

An ***adverse event*** for a device is defined as “untoward medical occurrence”. An adverse event is an untoward occurrence that is temporally associated with, but not necessarily related to or caused by, the use of the device If the untoward medical occurrence does not involve a subject, only occurrences related to the investigational device are included in the definition and handled by the Sponsor’s adverse event system.

A ***serious adverse event*** is defined as any untoward medical occurrence that meets the following criteria:

1. Results in death (i.e., the AE actually causes or leads to death)
2. Is life-threatening (i.e., an AE that, in the opinion of the Investigator, places the subject at immediate risk of death)
3. Requires in-patient hospitalization or prolongs an existing hospitalization (i.e., the AE requires hospitalization lasting at least 24 hours or prolonged hospitalization beyond the expected amount of time; hospitalizations for scheduled medical or surgical procedures to conduct scheduled treatments or routine examinations of SAEs do not meet these criteria)
4. Results in persistent or significant disability or incapacity (i.e., the AE causes substantial disruption in the ability of the subject to carry out normal activities)
5. Is a congenital anomaly or birth defect in the infant/ newborn of a mother that has been exposed to the research compound
6. Is considered by the Investigator to be significant medical event based on medical criteria (e.g., puts the subject at risk or may require medical or surgical intervention to prevent one of the aforementioned results)

The seriousness must be evaluated independently from the severity when documenting the AEs on the CRF.

Additionally, important medical events that may not result in death, be life threatening, or require hospitalization may be considered SAEs when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

A ***life threatening adverse event*** is any AE that places the subject at immediate risk of death from the event as it occurred. A life-threatening event does not include an event that might have caused death had it occurred in a more severe form but that did not create an immediate risk of death as it actually occurred.

Hospitalization is to be considered only as an overnight admission. Hospitalization or prolongation of a hospitalization is a criterion for considering an AE to be serious. In the absence of an AE, the participating investigator should not report hospitalization or prolongation of hospitalization on a form.

In addition, a hospitalization planned before the start of the study for a preexisting condition that has not worsened does not constitute an SAE (e.g. elective hospitalization after the procedure was performed and before study completion).

Disability is defined as a substantial disruption in subject's ability to conduct normal life functions.

17.3 Reporting of Serious Adverse Events

This section will address the reporting of the serious adverse event to the Sponsor and/or their representatives.

In the event that any SAEs occur during this study, the Investigator will notify the Sponsor or the Sponsor's safety representative via fax or phone immediately after becoming aware of the incident.

The Investigator will fax the SAE Report Form, and other documentation regarding the SAE to the Sponsor or the Sponsor's safety representative. The Investigator will promptly provide follow-up information requested by the Sponsor or the Sponsor's safety representative.

17.4 Collecting, Recording and Reporting Adverse Events

Adverse events will be recorded from the time a subject has signed the ICF until the subject terminates from the study. The Investigator is responsible for ensuring that all AEs are observed and reported during the study on the corresponding AE page of the CRF.

The Investigator will collect AE data at all stages of subject evaluation during the study. AEs will be recorded stating the duration (i.e., onset and resolved dates) of the event, the intensity, the relationship to the device, the relationship to the surgical procedure, action taken, the outcome, the seriousness, regulatory criterion, if any, and the presumed association with the study.

Note: The AE must be recorded on the AE page of the CRF. Each AE should be marked appropriately on the AE page as to whether it is serious. An SAE must be reported to the Sponsor or the designated safety personnel as soon as possible after the Investigator has become aware of its occurrence.

The causal relation between an AE and the study device will be determined by the investigator on the basis of his or her clinical judgment and the following definitions:

- ***Definitely related:*** Event can be fully explained by administration of the study device.
- ***Possibly related***: Event may be explained by administration of the study device or by the subject's clinical state or other agents/therapies.
- ***Not related***: Event can be fully explained by the subject's clinical state or other agents/therapies.

When assessing the relationship between the study device and an AE, the following should be considered:

1. Temporal relationship between the administration of the study device and the AE;
2. Biological plausibility of relationship;
3. Subject's underlying clinical state;

4. When applicable, whether the AE abates on discontinuation of the use of the study device.

SAEs that are not study related may nevertheless be considered by the participating investigator or the medical monitor (or designee) to be related to the conduct of the clinical study, i.e., to a subject's participation in the study. For example, a protocol-related SAE may be an event that is related to another non-test procedure required by the protocol.

The following definitions should be used when determining the severity of an AE.

- ***Mild:*** The AE is noticeable to the subject but does not interfere with activity.
- ***Moderate:*** The AE interferes with routine activity but responds to symptomatic therapy or rest.
- ***Severe:*** The AE significantly limits the subject's ability to perform activities despite symptomatic therapy.

18. STUDY SUSPENSION, TERMINATION, AND COMPLETION

The Sponsor may suspend or terminate the study or part of the study at any time for any reason. If the investigator suspends or terminates the study, the investigator will promptly inform the Sponsor and the IRB and provide them with a detailed written explanation. Upon study completion, the investigator will provide the Sponsor, IRB, and regulatory agency with final reports and summaries as required by regulations. The investigator must submit a written report to the Sponsor and the IRB within three months after the completion or termination of the study. Study termination and follow-up will be performed in compliance with the Sponsor's or designee's standard procedures.

18.1.1 Termination by the Sponsor

The Sponsor may terminate the study, or the study site, at any time for any of the following reasons:

1. Failure to enroll subjects
2. Protocol violations
3. Inaccurate or incomplete data
4. Unsafe or unethical practices
5. Questionable safety of the study device
6. Suspected lack of appropriateness of the study device
7. Administrative decision

18.1.2 Termination by the Investigator

If the investigator terminates the study prematurely, the investigator must provide the IRB and the Sponsor with a written statement describing why the study was terminated prematurely. Prompt compliance with this requirement is essential so that the Sponsor may comply with its regulatory obligations.

19. PROTOCOL AMENDMENTS

Any change in the study plan requires a protocol amendment. An investigator must not make any changes to the study without IRB and Sponsor approval except when necessary to eliminate apparent immediate hazards to the subjects. A protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately, but the change must then be documented in an amendment, reported to the IRB and Sponsor within 5 working days, and submitted to the appropriate regulatory agency in the required time frame.

20. QUALITY CONTROL AND ASSURANCE

The Sponsor performs quality control and quality assurance checks on this clinical study in accordance with regulatory agency data integrity requirements and data management SOPs. Before enrolling any subjects in the study, the clinical study monitor and the Investigator(s) will review the protocol, the IB, the CRF instructions, the procedure for obtaining informed consent and the procedure for reporting AEs and SAEs.

A qualified representative of the Sponsor monitors the conduct of the study by visiting the site, by contacting the site by telephone, and sending emails. During the visits, information recorded on the CRFs is verified against source documents. The Sponsor's medical monitor or designee reviews the data for safety information. The Sponsor's clinical data associates or designees review the data for legibility, completeness, and logical consistency.

Additionally, the Sponsor's clinical data associates or designees use automated validation programs to help identify missing data, selected protocol violations, out-of-range data, and other data inconsistencies. Access to the database shall be limited to appropriate personnel, per 21 CFR Part 11 compliance.

21. DIRECT ACCESS, DATA HANDLING, AND RECORD-KEEPING

21.1 Investigator

The investigator will permit study-related monitoring, audits, IRB review, and regulatory inspections by providing direct access to original source data and documents. All subject information will be recorded on source documents. The CRFs must be fully completed and include all required data for all subjects enrolled. All CRF data must be submitted to the Sponsor throughout and at the end of the study.

21.2 Data Handling

21.2.1 General Instructions for Data Collection

Data will be collected on CRFs. Data will be collected either via paper or electronic CRFs. The Investigator will be responsible for the accuracy and completeness of the CRFs. When submitted electronically, CRF completion will be tracked by the user name and password of the Investigator or designee. This electronic data collection utility, an image archive, will be tested, validated, and documented prior to data collection and submission. All electronic systems are validated according to 21 CFR Part 11 and Good Clinical Practice standards. Appropriate audit trials exist on both the front and back end of the data management systems. Back-up files are maintained by the Sponsor in accordance with 21 CFR Part 11. Access to investigative folders will be controlled through user name and passwords, and each site will have access to their electronic folder throughout the course of the study.

21.2.2 Data Submission

Completed Case Report Forms must be sent directly to the Sponsor for data load, validation and analysis. Every effort should be made to ensure data submission to the Sponsor within 30 days of visit completion.

21.2.3 Quality Assurance of Data and Monitoring

Cayenne Medical Inc. or its designee will monitor and ensure this investigation is conducted in accordance with the signed Clinical Trial Agreement, the Investigational Plan, conditions imposed by the Institutional Review Boards and the requirements of Title 21, Code of Federal Regulations, Part 50, 54, 56, and 812.

The Sponsor will conduct a site initiation visit to ensure the investigators and staff have adequate time and resources to implement and follow the investigational plan, and ensure the investigators have access to the target patient population under study. Prior to initiation of the study, the investigator must have a fully executed Clinical Trial Agreement and IRB/EC approval of this investigational plan and informed consent.

During the investigation, the Sponsor will conduct periodic monitoring visits and maintain contact with the investigators and staff to monitor investigational plan compliance and evidence of subject related adverse events. The clinical study manager will report any non-compliance with the signed Clinical Trial Agreement, investigational plan, applicable regulations, or any condition of approval imposed by the reviewing IRB/EC to the Sponsor.

CRFs will be routinely reviewed by the Sponsor for completeness and accuracy and any evidence of increased subject risk. When any discrepancies are identified, they will be addressed with the investigator or qualified designee.

21.2.4 Study Site Personnel Changes

If an investigator retires, relocates, or otherwise withdraws from conducting the study, the investigator must notify the Sponsor to agree upon an acceptable storage solution. The IRB will be notified with the appropriate documentation.

21.2.5 Adverse Event Reporting

The investigator agrees to report all AEs to the Sponsor as described in the Adverse Events section. Furthermore, the investigator is responsible for ensuring that any co-investigator or sub-investigator promptly brings AEs to the attention of the investigator. If applicable, the investigator also is responsible for informing the participating IRB of any SAEs.

21.2.6 Review of Source Records

Source documents will be maintained on site and will consist of but not be limited to: handwritten progress notes, completed Sponsor provided template source documents, subject diary, dictated results, study logs, and study-specific site-generated documents.

The investigator agrees that qualified representatives of the Sponsor and regulatory agencies will have the right, both during and after this study, to conduct inspections and to audit and review medical records pertinent to the clinical study as permitted by the regulations. Subjects will not be identified by name, and confidentiality of information in medical records will be preserved. The confidentiality of the subject will be maintained unless disclosure is required by regulations. Accordingly, the following statements (or similar statement) will be included in the informed consent document.

Representatives of regulatory agencies, IRBs, the Sponsor, and your personal physician may review your medical records and all information related to this study as permitted by law. Identifying information will not appear on any record received by the Sponsor. Subject identity will remain confidential unless disclosure is required by law.

21.2.7 Monitoring of the Study

This study is monitored by a representative of the Sponsor. Site visits may be made before the study begins, at regular intervals during the study, and at the study closeout. Communication by telephone and mail and e-mail may be used as needed to supplement site visits. The investigator and study site will permit monitoring, audits, IRB review, and regulatory inspection by providing authorized personnel from the Sponsor, its representatives, the IRB, the FDA and other appropriate regulatory agency direct access to all study data. Any party with direct access should take reasonable precautions to maintain the confidentiality of the study subjects and Cayenne Medical Inc.'s proprietary information. The purpose of the site visits is to verify the following:

1. Adherence to the protocol. (The investigator should document and explain any deviation from the approved protocol.)

2. The completeness and accuracy of the CRFs. Adequate time and space for these visits should be allocated by the investigator.

3. Compliance with regulations. The verification will require comparison of the source documents to the CRFs.

4. All subject records have complete, accurate and plausible ICFs and all study-specific logs.

22. PUBLICATIONS POLICY

The Sponsor will be responsible for determining when the study results should be published. The Sponsor will work jointly with the investigators to publish information. The investigator shall not submit a publication to journals or professional societies without agreement and prior written approval of the Sponsor.

REFERENCES

1. Patel, Manish. M.D. *Biomechanical Pullout Strength and Cyclic Testing of the SureLock™ All Suture Anchors*.

2. Barber et al. *Cyclic Load Testing of Biodegradable Suture Anchors Containing 2 High-Strength Sutures*. Arthroscopy 2007 4:355-360