Persona™ Outcomes Led Assessment Research
in Total Knee Arthroplasty

POLAR –TKA STUDY

PROSPECTIVE MULICENTER STUDY OF
***PERSONA*™ KNEE SYSTEM**

Protocol # CSU2012-10K
United States

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STUDY/CONTACT INFORMATION SHEET

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PROTOCOL NUMBER:	CSU2012-10K
STUDY TYPE:	Post Market
STUDY SPONSOR:	Zimmer, Inc 1800 West Center Street Warsaw, IN 46580 Ph: 800-613-6131
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I. Study Synopsis

TITLE:	*Persona* Outcomes Led Assessment Research in Total Knee Arthroplasty (POLAR Study)
SPONSOR:	Zimmer Inc., Warsaw, IN
PROTOCOL NUMBER	CSU2012-10K
STUDY OBJECTIVES	The primary objective of this study is to obtain implant survivorship and clinical outcomes data for commercially available *Persona* fixed bearing implants used in primary total knee arthroplasty. The assessments will include: 1. Implant survivorship based on removal of a study device. 2. Safety based on incidence and frequency of adverse events. 3. Clinical performance measured by overall pain and function, quality of life data, radiographic parameters and survivorship.
TARGET POPULATION:	Patients qualifying for primary total knee arthroplasty who meet the inclusion/exclusion criteria for study participation
STUDY DESIGN:	Prospective multicenter, non-controlled study of commercially available Zimmer *Persona* fixed bearing knee components
STUDY TYPE:	Post-market
SAMPLE SIZE:	A maximum of 15 U.S. sites contributing a maximum of 100 implanted Persona knees per site
LENGTH OF STUDY:	Five year study Follow-up clinical visits include 6 weeks, 6 months, 1 year, 2, 3, 4, and 5 years post-op.

INCLUSION/EXCLUSION CRITERIA:	INCLUSION CRITERIA: 1. Patient is 18 to 75 years of age, inclusive 2. Patient qualifies for a primary total knee arthroplasty based on physical exam and medical history, including diagnosis of severe knee pain and disability due to at least one of the following: a. Rheumatoid arthritis, osteoarthritis, traumatic arthritis, polyarthritis b. Collagen disorders and/or avascular necrosis of the femoral condyle c. Post-traumatic loss of joint configuration, particularly when there is patellofemoral erosion, dysfunction or prior patellectomy d. Moderate valgus, varus, or flexion deformities e. The salvage of previously failed surgical attempts that did not include partial or total knee arthroplasty of the ipsilateral knee 3. Patient has participated in this study-related Informed Consent process 4. Patient is willing and able to provide written Informed Consent by signing and dating the IRB or EC approved Informed Consent form 5. Patient is willing and able to complete scheduled study procedures and follow-up evaluations 6. Independent of study participation, patient is a candidate for commercially available *Persona* fixed bearing knee components implanted in accordance with product labeling EXCLUSION CRITERIA: 1. Patient is currently participating in any other surgical intervention studies or pain management studies 2. Previous history of infection in the affected joint and/or other local/systemic infection that may affect the prosthetic joint 3. Insufficient bone stock on femoral or tibial surfaces 4. Skeletal immaturity 5. Neuropathic arthropathy 6. Osteoporosis or any loss of musculature or neuromuscular disease that compromises the affected limb 7. Stable, painless arthrodesis in a satisfactory functional position 8. Severe instability secondary to the absence of collateral ligament integrity 9. Rheumatoid arthritis *accompanied* by an ulcer of the skin or a history of recurrent breakdown of the skin 10. Patient has a known or suspected sensitivity or allergy to one or more of the implant materials 11. Patient is pregnant or considered a member of a protected population (e.g., prisoner, mentally incompetent, etc.) 12. Patient has previously received partial or total knee arthroplasty for the ipsilateral knee

STUDY DEVICE:	Commercially available *Persona* fixed bearing knee components implanted in accordance with product labeling
OUTCOMES MEASURES:	2011 Knee Society Score EQ-5D Forgotten Joint Score
PERFORMANCE ASSESSMENTS:	Pain and function Quality of life Radiographic parameters Survivorship
STATISTICAL REPORTING:	Performance will be evaluated for pain, function, quality of life, and survivorship. Data will be summarized descriptively additional to evaluation of data on surgical technique and instrumentation. Categorical data (e.g., gender or race) will be summarized using counts and percentages with 95% Confidence Interval (CI) limit over the time period of interest. Continuous data, such as age, will be summarized by using means, medians, SD, minimum, maximum, and 95% CI over the time period of interest. Implant survival and return to function will be summarized using a Kaplan-Meier method and presented with rates (as percentages) and CI. Routine summaries of complication data is represented by frequencies and percentages. Sample size is based on a longitudinal data collection model and using survivability as the primary endpoint of interest. The attrition rate is assumed to be 10%

This protocol is written based on guidelines from ISO 14155 Standard for Clinical Investigation of Medical Devices For Human Subjects – Good Clinical Practice [(i)] and the ICH Guideline on Good Clinical Practice[(ii)], and is in accordance with US Code of Federal Regulations 21 CFR Parts 11, 50 and 56 [(ii)]

II. Data Collection Overview

The following table indicates the necessary case report forms to be completed at the given time point:

Form Name	Pre-op	Surgical & Immediate Post-Surgical	6 weeks	6 months	1 year	Years 2, 3, 4, 5 Post-Surgical
Informed Consent	X					
Inclusion/Exclusion Criteria	X					
Demographic Evaluation	X					
Operative Information		X				
Surgical Device Information		X				
Discharge Summary		X				
Physical Exam	X		X	X	X	X
FJS-12 (Forgotten Joint Score)			●	●	●	●
EQ-5D	●		●	●	●	●
KSS - Surgeon completed	X		X	X	X	X
KSS – Patient completed	●		●	●	●	●
Physician Assessment of Post-op Radiographs			X	X	X	X
Adverse Event Report		★	★	★	★	★
Protocol Deviations	★	★	★	★	★	★
Study Completion	★	★	★	★	★	★
Independent Radiographic Review			♦	♦	♦	♦

X Completed by Investigator or Designee
● Completed by patient
★ Completed by Investigator or Designee as applicable
♦ Independent radiographic review may be performed by Sponsor's designee, if applicable at discretion of Sponsor

The following table indicates the necessary case report forms required to be completed for revision patients:

FORM NAME	REVISION (as applicable)	COMMENTS
Physician Assessment of Post-op Radiographs	★	Mark the "pre-revision" exam period.
Adverse Event Report	★	Document adverse event resulting in the revision
Study Completion	★	Complete indicating "Study Prosthesis Removed" under Study Completion Status.

★ Completed by Investigator or designee as applicable

III. Introduction and Purpose

Osteoarthritis (OA) is the most common type of arthritis causing considerable disability across broad populations. The economic burden of arthritis, specifically osteoarthritis is enormous with an estimated cost of $60 billion in the United States and expected to increase to $100 billion by 2020.[1,2] The knee joint is the most common joint to develop OA and total knee arthroplasty (TKA) is the most frequently performed joint arthroplasty procedure for this condition.[3,4] With an increase in the prevalence of arthritis, obesity, and old age, a further demand for TKA is projected to increase substantially over the next few years.[5-9] In 2005, approximately 523,000 TKAs were performed nationally.[10] The American Academy of Orthopedic Surgeons (AAOS) and Kurtz et al,[11] have provided projections for future demand of TKA. In 2002, the AAOS had suggested an annual replacement load of 474,000 by the year 2030. In 2007, Kurtz et al,[11] described an annual demand of 3.5 million by 2030. While these projections vary widely, both suggest a strong increase in demand for TKA, prompting significant interest from surgeons, healthcare institutions and orthopedic device manufacturers interested to better understand the future technological and economic burden of TKA.

Although, TKA has demonstrated effectiveness with substantive and sustained improvement in quality of life for individuals with moderate to severe osteoarthritis,[12,13] functional performance in patients 1 year after TKA remains lower than for healthy adults, with reports of an 18% slower walking speed, 51% slower stair-climbing speed, and deficits of nearly 40% in quadriceps strength.[14] Additionally, certain limitations in knee design systems require surgeons to accept compromises which can result in surgical inefficiencies and challenges in seizing desired outcomes.[15-19] Patient expectations and an ever emerging population with active lifestyle also add a new requirement and need for innovative designs that bring advantages over traditional implants. Personalized implants with critical features of natural movement, contoured shape, and unique anatomic and physiologic composition can address these requirements. The current concepts in TKA warrant a personalized orthopedics initiative by offering a finer ability in identifying and precisely addressing the unique needs of patients. It is through this introduction of high fidelity implants, morphologic designs and intelligent instrumentation that each patient's knee can be distinctively and accurately reconstructed, allowing for clinical outcomes to be better optimized. Furthermore, such personalized systems will empower the surgeon to advance performance by providing a leading design that efficiently accommodates surgeons' intraoperative needs with minimizing surgical trade-offs and maximizing efficiency.

To address these clinical challenges and methodologically address new implant characteristics, a prospective, multi-center, longitudinal data collection model is being proposed. The objective of this study is to determine clinical performance/ outcomes and implant survivorship for commercially available *Persona®* fixed bearing implants used in primary total knee arthroplasty.

IV. Study Objectives

The objective of this study is to obtain clinical performance (outcomes) data and survivorship for commercially available *Persona* fixed bearing knee components implanted in primary total knee arthroplasty. This will be done by analysis of validated outcome measurement tools, radiographs and adverse event data.

The assessments will include:

1. Implant survivorship based on removal of a study device
2. Safety based on incidence and frequency of adverse events
3. Clinical performance measured by overall pain and function, quality of life data, radiographic parameters and survivorship

V. Study Design

This is a prospective, multicenter, non-controlled clinical study designed to facilitate the collection and evaluation of pain, function, quality of life, radiographic assessment, and adverse event data. A minimum of six U.S. sites will contribute to this study. Maximum enrollment per site will not exceed 100 implanted knees. Each Investigator will be skilled in total knee arthroplasty and experienced implanting the devices included in this study.

Each Principal Investigator will be responsible for obtaining Institutional Review Board (IRB) or Ethics Committee (EC) approval as required prior to conducting the study. In order to avoid potential selection bias, each Investigator will offer study participation to each consecutive patient presenting as a candidate for primary total knee arthroplasty using the commercially available (FDA cleared) *Persona* fixed bearing knee system. Candidates who express interest in study participation will be offered Informed Consent. All potential study subjects will be required to participate in the Informed Consent process and will not be considered enrolled in the study until the candidate has signed and dated the IRB/EC approved patient Informed Consent. Study data cannot be collected until the candidate has completed the informed consent process and signed and dated the IRB or EC approved Informed Consent.

All study subjects will undergo preoperative clinical evaluations prior to their total knee arthroplasty. The post-operative clinical and radiographic evaluations will be conducted at 6 weeks, 6 months, 1 year, 2, 3, 4, and 5 years.

The Investigator will review radiographs at each clinical evaluation interval to ensure radiographic evidence of adverse events is documented and reported to the IRB or EC and Sponsor as required. At Sponsor's discretion, Sponsor may request copies of these radiographs for independent radiologic review. Sponsor may request one central reviewer for all radiographs independent of the surgeon and institution.

VI. Study Population

Study population for primary statistical analysis will be comprised of males and females who require primary total knee arthroplasty and satisfy the inclusion/exclusion criteria outlined in this section of the protocol. In order to avoid potential selection bias, each Investigator will offer study participation to each consecutive patient presenting as a candidate for primary total knee arthroplasty using the commercially available (FDA cleared) *Persona* fixed bearing knee system. Candidates who express interest in study participation will be offered Informed Consent.

A. Inclusion Criteria

1. Patient is 18 to 75 years of age, inclusive
2. Patient qualifies for a primary total knee arthroplasty based on physical exam and medical history, including diagnosis of severe knee pain and disability due to at least one of the following:
    a. Rheumatoid arthritis, osteoarthritis, traumatic arthritis, polyarthritis
    b. Collagen disorders and/or avascular necrosis of the femoral condyle
    c. Post-traumatic loss of joint configuration, particularly when there is patellofemoral erosion, dysfunction or prior patellectomy
    d. Moderate valgus, varus, or flexion deformities
    e. The salvage of previously failed surgical attempts that did not include partial or total knee arthroplasty of the ipsilateral knee
3. Patient has participated in a study-related Informed Consent process
4. Patient is willing and able to provide written Informed Consent by signing and dating the IRB/EC approved Informed Consent form
5. Patient is willing and able to complete scheduled study procedures and follow-up evaluations
6. Independent of study participation, patient is a candidate for commercially available *Persona* fixed bearing knee components implanted in accordance with product labeling

B. Exclusion Criteria

1. Patient is currently participating in any other surgical intervention studies or pain management studies
2. Previous history of infection in the affected joint and/or other local/systemic infection that may affect the prosthetic joint
3. Insufficient bone stock on femoral or tibial surfaces
4. Skeletal immaturity
5. Neuropathic arthropathy
6. Osteoporosis or any loss of musculature or neuromuscular disease that compromises the affected limb
7. Stable, painless arthrodesis in a satisfactory functional position
8. Severe instability secondary to the absence of collateral ligament integrity
9. Rheumatoid arthritis *accompanied by* an ulcer of the skin or a history of recurrent breakdown of the skin
10. Patient has a known or suspected sensitivity or allergy to one or more of the implant materials
11. Patient is pregnant or considered a member of a protected population (e.g., prisoner, mentally incompetent, etc.)
12. Patient has previously received partial or total knee arthroplasty for the ipsilateral knee.

VII. Study Device Information

Persona knee components included in this study are commercially available (FDA cleared) in fixed bearing left and right side configurations and various component sizes to accommodate anatomical variation. Fixed bearing components may be configured for use in posterior cruciate-retaining, cruciate-sacrificing, or cruciate-substituting knee arthroplasty procedures.

They are intended for long-term implantation in accordance with product labeling. Please refer to the package insert for additional information and instructions.

VIII. Study Procedures

A. Offer Study Participation

Study participation will be offered to each consecutive patient presenting as a potential candidate for primary total knee arthroplasty using the commercially available (FDA cleared) *Persona* fixed bearing knee system. Candidates who express interest in study participation will be offered Informed Consent. Prior to patient enrollment or any further patient evaluation for study eligibility, the patient must participate in the Informed Consent process and sign and date the IRB or EC approved Informed Consent.

B. Informed Consent Process

For candidates that express interest, the Investigator or Designee will describe relevant study information, including the purpose, procedures, possible risks, and potential benefits associated with study participation. The Investigator or Designee will also review, along with the candidates, the Informed Consent approved by both the governing IRB or EC and the study Sponsor. Candidates shall have sufficient time to read and understand the IRB or EC approved Informed Consent and discuss whether they wish to participate in the study. Candidates will be asked to acknowledge whether all of their questions and concerns have been addressed to their satisfaction. Any questions that candidates may have will be addressed appropriately by the Investigator or Designee. Candidates will be further instructed that they are free to obtain additional information from the Investigator or Designee at any time, that they are free to decline participation, and that they are free to withdraw their consent and discontinue their participation at any time without prejudice.

After completing the Informed Consent process, candidates who agree to enter the study must sign and date the IRB or EC approved Informed Consent. The Informed Consent must be signed and dated prior to the date of the study surgery. For bilateral TKA candidates that agree to enroll for both operative sides, a separate Informed Consent must be signed and dated for each operative side.

A copy of the signed Informed Consent must be provided to the study subject. The original signed Informed Consent is to be filed in the subject's medical record, study subject binder, or regulatory binder.

Study data will not be collected until the Informed Consent has been signed and dated. If the candidate does not wish to participate (does not sign and date the Informed Consent), data for that candidate will not be collected for this study.

C. Informed Consent Log

An Informed Consent Log (Appendix C) will be maintained at the site throughout the course of the study. The purpose of the Informed Consent Log is to provide documentation that all enrolled study subjects underwent the Informed Consent process, signed and dated the IRB or EC approved Informed Consent, and were provided with a copy of the fully executed

consent with all required signatures. All candidates who sign and date the approved Informed Consent for the study must be entered in the log. If a subject signs and dates additional Informed Consent(s) after enrollment (e.g., due to a protocol amendment, protocol revisions, etc.), subsequent signings will also be recorded in the log. The Informed Consent Log will be filed in the site Regulatory Binder for the study.

D. Subject Enrollment

Once the Informed Consent has been signed and dated by the subject, the subject will be considered enrolled in the study. A unique case identification number (Case ID) will be assigned to each participating subject/knee (bilateral subjects will be assigned a unique case ID number for each knee). This unique case ID number will be used throughout the study for identification. Case ID numbers will be assigned consecutively in ascending order per site, with the starting number for a given site defined by Sponsor.

E. Determination of Eligibility

Once Informed Consent has been obtained, the subject's eligibility to continue study participation will be determined by the study inclusion/exclusion criteria. This may include an interview to assess significant subject medical/surgical history, history of present illness/injury, evaluation of present pain and functional capacity, and a radiographic assessment. Evaluation of the inclusion/exclusion criteria will be documented on the Inclusion/Exclusion Criteria case report form. Subjects that do not meet all inclusion/exclusion criteria will be terminated from the study and no further study data will be collected. A Study Completion form will be completed and the reason for termination must be specified on the form. These subjects will be excluded from the primary statistical analysis for this study.

F. Monitor Log

The Site Monitoring Visit Log (Appendix C) will be maintained throughout the course of the study. The log will contain the visit date, monitor name/signature and the purpose of the visit (i.e. site initiation, onsite interim monitoring (as applicable), site close-out, etc.). The site monitoring visit log will be filed in the site Regulatory Binder for the study.

G. Delegation of Authority (Site Signature Log)

A Site Signature Log (Appendix C) will be maintained throughout the study and will contain the names, initials, signatures and study responsibilities of all site personnel/designees involved in study procedures and data collection. The Site Signature Log will be filed in the site Regulatory Binder for the study.

H. Baseline/Pre-operative Assessment

Baseline/pre-operative data will be collected on the following case report forms:

1. Inclusion/Exclusion Criteria
2. Demographic Evaluation
3. Physical Exam
4. EQ-5D
5. Knee Society Score
    a. Surgeon completed
    b. Patient completed
6. Protocol Deviations (as applicable)
7. Study Completion (as applicable)

I. Surgical Technique

Standard operative procedures will be followed and all surgical procedures will be performed under aseptic conditions. Investigators will implant all commercially available *Persona* fixed bearing components and any other compatible products in compliance with corresponding labeling requirements and in accordance with appropriate surgical technique(s).

J. Intention to Treat

Subjects who are enrolled in the study with an intention to treat (i.e. underwent the study Informed Consent process, signed and dated the Informed Consent, and met the study inclusion/exclusion criteria), but do not undergo the study surgery due to subject withdrawal, investigator withdrawal, or any other reason(s), will be terminated from the study. A Study Completion form will be completed and the reason for termination must be specified on the form. These subjects will be excluded from the primary statistical analysis for this study.

K. Surgical and Immediate Post-surgical Procedures (Data Collection)

Surgical and immediate post-surgical data will be collected on the following case report forms:

1. Operative Information
2. Surgical Device Information
3. Discharge Summary
4. Adverse Event Report (as applicable)
5. Protocol Deviations (as applicable)
6. Study Completion (as applicable)

Post-surgical management for study subjects will follow the investigator's standard of care for patients undergoing total knee arthroplasty (e.g. prophylactic antibiotic therapy, prevention of deep vein thrombosis, prevention of pulmonary embolism, etc.).
Post-surgical rehabilitative therapy will be as prescribed by the investigator.

L. Post-operative Follow-up Procedures (Data Collection)

Post-operative clinical evaluations/assessments will be conducted at the following visit intervals:

Clinical Interval	Interval Window in Days Post-op*	Approximate Window in Weeks or Months Post-op*
6 weeks	17 to 90 days	-4 weeks / +7 weeks
6 months	91 to 244 days	-3 months / +2 months
1 year	245 to 547 days	-4 months/ +6 months
2 years	548 to 912 days	-/+ 6 months
3 years	913 to 1277 days	-/+ 6 months
4 years	1278 to 1642 days	-/+ 6 months
5 years	1643 to 2007 days	-/+ 6 months

*Visit(s) outside of window will be determined based on Days Post-op

Post-operative clinical data will be collected on the following case report forms:

1. Physical Exam
2. FJS-12 (Forgotten Joint Score)
3. EQ-5D
4. Knee Society Score
    a. Surgeon completed
    b. Patient completed
5. Physician Assessment of Post-op Radiographs
6. Adverse Event Report (as applicable)
7. Protocol Deviations (as applicable)
8. Study Completion (as applicable)

Subjects will be followed post-operatively for up to 5 years. Unless the study is otherwise closed, data will continue to be collected until the subject completes the study per the protocol, voluntarily withdraws from the study, is withdrawn from the study by the investigator, is lost to follow-up, undergoes revision to remove a study device, or expires. See Management of Incurrent Events (Section IX, Subsection D of this protocol) for additional details. Reason(s) for study completion must be documented on the Study Completion case report form.

M. Minimization of Subjects Lost to Follow-up

Subject follow-up is extremely important for the conduct of a clinical study, and the expectation is to maintain the highest possible rate of follow-up compliance throughout this study. At each follow-up interval, subjects should be counseled on the importance of completing future study follow-up intervals.

N. Radiographic Definitions and Methods

All postoperative radiographic evaluations performed according to the protocol will be reviewed by the Investigator at the time of the evaluation and documented using the Physician Assessment of Post-op Radiographs case report form. This includes documentation of any significant radiographic findings. In addition, an Adverse Event Report case report form must be completed for those findings indicated by an asterisk on the Physicians Assessment of Post-op Radiograph case report form, or for any other findings identified as an adverse event.

1. Required radiographic views
   Standing anteroposterior (AP) and standard lateral radiographs of the operative knee are required to be captured at the 6 week, 6 month, 1 year, 2 year, 3 year, 4 year, and 5 year follow-up visits.

   Radiographs should have similar exposure and must show the entire study device and surrounding bone. For consistency, every effort should be made to capture all radiographic views for a given subject using the same institution throughout the study. However, radiographs captured at a different institution may be used for the study, provided they meet required study specifications and are captured within the required interval window. The investigative site will retain copies (hard copy/CD/digital) of all radiographs referenced for the study.

2. Submission to Sponsor
   At Sponsor's discretion, study radiographs may be requested from the sites for independent radiographic review and assessment of appropriate parameters.

O. Recommended Revision Procedure

See Management of Incurrent Events (Section IX, Subsection D of this protocol)

IX. Reporting

The management of all study data received by Sponsor will be the responsibility of Sponsor or its Designee. The use or disclosure of all protected health information will comply with the Health Insurance Portability and Accountability Act (HIPAA). All information will be treated with strict adherence to professional standards of confidentiality and will be filed by Sponsor under adequate security and restricted accessibility by clinical personnel. All electronic systems used to create, modify, maintain, or transmit study records will be validated according to 21 CFR Part 11[ii]. Reports and communications relating to study subjects will typically identify each subject only by the subject's initials, assigned study subject Case ID number, date of surgery, operative side, and date of birth.

A. Prior to Initiation of the Study

1. Clinical Trial Agreement (CTA)
   A fully executed (signed by all required parties) CTA must be on file with Sponsor prior to any investigator participating in this study.

2. Institutional Review Board/Ethics Committee Protocol Approval
   This study protocol must be submitted to and approved by the Investigator's Institutional Review Board (IRB) or Ethics Committee (EC). A copy of the IRB or EC approval letter must be submitted to Sponsor. The letter should identify the following:
   - Protocol name and/or number
   - Date of IRB or EC meeting (if available)
   - Date of approval
   - Date of expiration
   - Signature of IRB or EC

3. Informed Consent
   A Sponsor-approved Informed Consent document (Appendix A Sample) will be provided along with the study protocol for IRB or EC submission and approval. If the IRB or EC requires revisions to the provided Informed Consent, the requested revisions must be submitted by the Investigator to Sponsor for review and approval. Once Sponsor has reviewed and approved the revision, the Informed Consent will be re-submitted to the IRB or EC for final review and approval. A copy of the final IRB or EC approved Informed Consent form (ICF) must be submitted to Sponsor.

B. Clinical Data Collection/Submission

1. Summary of Case Report Form Data Collection
   Study data will be collected on study-specific Case Report Forms (CRFs) provided by Sponsor. For subjects having bilateral knee replacement, separate case report forms must be completed for each operative side.

   The following CRF guidelines should be followed:

   - Complete carefully and accurately.
   - Complete header information consistently across all case report forms for each individual study subject.
   - Use the study subject's initials in header section.
   - Use the study subject's unique Case ID number assigned as instructed.
   - Do not provide information that is not requested on the CRFs.
   - Ensure that all fields are completed. For fields completed by the subject, efforts should be made to obtain any missing responses prior to the subject completing their visit.

2. Data Submission
   Completed CRFs will be submitted directly to Sponsor by electronic data capture and submission via a method approved by Sponsor. Every effort must be made to ensure data submission to Sponsor is made within 30 days of the visit completion.

3. Quality Assurance of Data
   The Investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor in the CRFs and in all required reports. Data reported on the CRF, which are derived from source documents, should be

consistent with the source documents or the discrepancies should be explained. All electronic systems used to create, modify, maintain, or transmit electronic study records will be validated according to 21 CFR Part 11[ii]. Sponsor will maintain quality control systems, in accordance with Sponsor's policies and procedures.

C. Reporting Requirements

1. Investigator Reporting Responsibilities
   The Investigator should ensure the accuracy, completeness, legibility, and timeliness of data reported to the Sponsor in accordance with this protocol. The Investigator or Designee will provide periodic reports to their IRB or EC as required to maintain IRB or EC approval throughout the study, and will provide any required final reporting to the IRB or EC upon study completion/termination. A copy of all IRB or EC re-approval letters must be submitted to the Sponsor. If the IRB or EC terminates or suspends its approval of the study, the Investigator or Designee will suspend study-related activities and will promptly notify the Sponsor. The Investigator should also promptly provide written reports to the Sponsor and the IRB or EC regarding any changes significantly affecting the conduct of the study, and/or increasing risk to the subjects.

2. Retention of Records
   Study records must be retained by the Investigator or Designee for a minimum of 2 years from the Investigator's study termination date, or per applicable regulatory and/or IRB or EC requirements (whichever time period is greater). Measures shall be taken to prevent accidental or premature destruction.

D. Management of Incurrent Events

1. Failure to Obtain Informed Consent
   Study data will not be collected until the Informed Consent has been signed and dated by the candidate. If a candidate does not wish to participate (does not sign and date the Informed Consent), data for that candidate will not be collected for this study.

2. Adverse Events
   An adverse event is any unfavorable or unintended sign, symptom, or disease associated with the use of the study device, whether or not related to the device. Adverse event is synonymous with complication or medical event.

   See Section IX, Subsection E of this protocol for additional information regarding adverse event classifications. All medical events, regardless of classification, are required to be reported on the Adverse Event Report case report form. The completed Adverse Event Report case report form must be submitted to Sponsor in a timely manner. The Investigator or Designee will also promptly provide Sponsor with any additional requested information required for Sponsor to comply with regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will also report applicable adverse event(s) to their IRB or EC.

3. Revision
   In the event that removal of one or more of the study knee components is necessary, the Investigator will determine the best treatment and/or revision method for the subject.

   Prior to revision surgery, the Investigator or qualified Designee must document any significant radiographic findings related to the need for revision on the Physician Assessment of Postop Radiographs case report form. An Adverse Event case report form must be completed for those findings indicated by an asterisk on the Physicians Assessment of Postop Radiograph case report form.

   Once the revision surgery has been completed, the Investigator or qualified Designee must complete an Adverse Event case report form as well as a Study Completion case report form terminating the subject from the study. For the study completion status, select "Study Prosthesis Removed". This procedure also applies to partial revisions such as polyethylene exchange.

4. Investigator Withdrawal
   The Investigator can choose to withdraw a subject from the study if the subject no longer meets study inclusion/exclusion criteria. The reason for the Investigator's withdrawal of the subject must be documented on the Study Completion case report form.

5. Subject Withdrawal
   Study subjects may choose to withdraw from the study at any time, for any reason. If possible, a final evaluation will be completed for any subject who no longer wishes to participate in the study. The reason for the subject withdrawal must be documented on the Study Completion case report form.

6. Lost to Follow-up
   A study subject will be considered lost to follow-up after they have missed a visit and attempts to locate and evaluate the subject using the procedure outlined below have failed. All attempts to contact the subject are to be documented in the subject's medical record and on the Study Completion case report form. Missed visit(s) also must be documented using the Protocol Deviations case report form. The first three contact attempts should be made by telephone, with additional attempts as outlined in the following table:

If	Then
a response is not received after three (3) phone calls	the Investigator or Designee should send a letter to the subject explaining the follow-up agreement per the Informed Consent, and requesting a response from the subject.
all attempts to contact the subject are unsuccessful or the subject is contacted and chooses to withdraw from the study	a Study Completion case report form will be completed and will specify the reason the subject is no longer participating in this study.

7. Protocol Deviations
   Investigators should not deviate from the study protocol. If a protocol deviation does occur, the deviation must be documented on the Protocol Deviation case report form and submitted to Sponsor. If applicable per their reporting requirements, the Investigator or Designee will also report applicable protocol deviations to their IRB or EC.

8. Study Termination
   Study subject participation is expected to end upon completion of the subject's 5-year follow-up visit unless the subject voluntarily withdraws from the study, is withdrawn from the study by the Investigator, is lost to follow-up, undergoes revision to remove a study device, or expires. Reason(s) for study completion must be documented on the Study Completion case report form.

   If Sponsor decides to terminate the study early, Sponsor will inform the Investigators of the reason for early study termination. It is the responsibility of the Investigators to inform their IRB or EC as applicable according to local and national laws/regulations.

9. Modification of the Protocol
   All amendments to this clinical protocol shall be agreed to by Sponsor and be recorded with a justification for the amendment prior to implementation. Approval of the applicable IRB or EC must be obtained prior to implementation, if required according to the local and/or national laws/regulations.

E. Medical Events/Adverse Events Definitions and Classifications

An adverse event is any unfavorable or unintended sign, symptom, or disease associated with the use of the study device, whether or not related to the device. Adverse event is synonymous with complication or medical event. All medical events, regardless of classification, are required to be reported on the Adverse Event Report case report form. The completed Adverse Event Report case report form must be submitted to Sponsor in a timely manner. The Investigator or Designee will also promptly provide Sponsor with any additional requested information required for Sponsor to comply with regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will also report applicable adverse event(s) to their IRB or EC.

1. Classification of the Event:
   Adverse Event (AE)[(i)]*:*
   An Adverse Event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device.

Serious Adverse Event (SAE)[(i)]**:**

A Serious Adverse Event is any adverse event that

a. led to death
b. led to serious deterioration in the health of the subject, that either resulted in
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function, or
    3. in-patient or prolonged hospitalization, or
    4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
c. led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.

Adverse Device Effect (ADE)[(i)]**:**

An Adverse Device Effect is an adverse event related to the use of a medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the medical device.

Serious Adverse Device Effect (SADE)[(i)]*:*

A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Sponsor is responsible for determining the final classification of adverse events.

If an Unanticipated Serious Adverse Device Effect (USADE) is identified by Sponsor, it will be promptly reported to concerned Investigators and regulatory authorities as required by applicable regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will report the USADE to their IRB or EC.

2. Intensity of Symptoms

Mild:

The subject is aware of the sign or symptom, but finds it easily tolerated. The event is of little concern to the subject and/or little clinical significance. The event is not expected to have any effect on the subject's overall health or well being.

Moderate:
The subject has discomfort enough to cause interference with or change in usual activities. The event is of some concern to the subject's health or well being and may require medical intervention and/or close follow-up.

Severe:
The event interferes considerable with the subject's usual activities. The event is of definite concern to the subject and/or poses substantial risk to the subject's health or well- being. The event is likely to require medical intervention and/or close follow-up and may be incapacitating or life threatening. Hospitalization and treatment may be required.

NOTE: The term "severe" refers to the intensity of the event and can be used with any event, without regard to whether or not it meets the criteria for being classified as "serious" or "unanticipated". For example, a subject can have a severe headache, but it is not a serious event.

3. Outcome Definitions
The outcome is in relationship to the Adverse Event, not the treatment rendered for the event (if any).

Resolved:
The adverse event has been resolved and/or no further treatment is required to treat the reported condition or illness.

Tolerated:
The adverse event will most likely never be resolved. The subject "tolerates" the illness or condition as a matter of life.

Pending:
Treatment or diagnostic studies were prescribed for the adverse event and the outcome of the adverse event is not yet known.

Study Withdrawal:
Due to the adverse event, the subject was withdrawn from the study.

Device Removal:
The adverse event resulted in the removal of a study device.

Reoperation of Affected Joint:
The adverse event resulted in reoperation of the study joint, but the reoperation did not include removal of a study device.

Death:
The outcome indicates the subject died as a direct result of the reported adverse event.

F. Monitoring of the Study

Prior to initiating the clinical study, Sponsor will conduct a site initiation visit to ensure the Investigator(s) and study staff understand the study protocol and requirements and have adequate time and resources to implement and conduct the study. Prior to study initiation, the Investigator must have a fully executed CTA and IRB or EC approval of the study protocol and the study Informed Consent.

During the course of the study, Sponsor will conduct periodic central monitoring and maintain contact with the study staff to monitor compliance and evidence of adverse events, in accordance with Sponsor's policies and procedures. Sponsor will address any identified non-compliance with the executed CTA, study protocol, and applicable regulatory requirements.

If onsite monitoring visit(s) are deemed appropriate by Sponsor, the Investigator will permit representatives of Sponsor's monitoring team to have direct access to inspect all source data/documents, study documents/binders, study subject case report forms, corresponding sections of study subject medical/hospital records, and any other documents relevant to the study. All Sponsor visits (including site initiation) will be documented using the Site Monitoring Visit Log (Appendix C).

X. Risk Analysis

This post-market clinical study is classified as minimal risk[(ii)] and there are no anticipated risks specific to study participation other than the potential loss of confidentiality. There are no experimental procedures in this study, and participation in this study is not anticipated to affect the medical treatment of enrolled subjects.

When used in accordance with product labeling, the risks associated with the use of *Persona* knee components are similar to those of standard, metal-on-polyethylene knee systems used for the same clinical indication or purpose. These risks are categorized below as either general surgical risks or risks associated with the total knee arthroplasty procedure/study device. Unanticipated adverse events can also occur.

A. General Surgical Risks

General surgical risks and post-operative adverse events can occur with any surgery and include, but are not limited to:

Anesthetic complications/reactions
Bleeding and/or excessive blood-loss
Transfusion reaction
Chronic Pain
Post-operative infection
Vascular injury
Delayed wound healing
Deep vein thrombosis (DVT)
Nerve injury
Death

B. Risks Associated with Total Knee Arthroplasty Procedure/Study Device

Potential adverse events associated with total knee arthroplasty include, but are not limited to:

Wear of the polyethylene articulating surface
Progressive bone resorption (osteolysis) as a result of foreign-body reaction to wear debris
Loosening of the prosthetic knee components
Fracture/damage of the prosthetic knee components
Soft tissue impingement or damage
Dislocation and/or joint instability
Malalignment of the prosthetic knee components
Bone fracture
Nerve damage
Swelling
Infection
Leg length discrepancies
Poor range of motion
Delayed wound healing
Temporary or permanent neuropathies
Pain
Cardiovascular disorders including venous thrombosis, pulmonary embolism, or myocardial infarction
Histological reactions resulting in inflammation
Metal sensitivity
Corrosion of metal components (the significance and long-term implications are uncertain and await further clinical evidence and evaluation)

Minimization of Risk

Investigators should refer to the package insert for additional information and instructions.

XI. Statistical Considerations

Performance of commercially available *Persona* fixed bearing knee components in primary total knee arthroplasty will be evaluated for pain, function, quality of life, and survivorship. Data collected in this study will be summarized descriptively and descriptive summaries will be the basis of any study reports issued. These summaries may be used for interim study reports and may also be used to support regulatory submissions, presentations, and/or publications. Additional surgical technique and instrumentation data may be collected and evaluated.

A. General Statistical Methods

Statistical methodology will consist of summarizing collected data descriptively. Categorical data (e.g., gender or race) will be summarized using counts and percentages, and 95% Confidence Interval (CI), over the time periods of interest. Continuous data, such as age, will be summarized by using means, medians, standard deviation, minimum, maximum, and 95% CI over the time periods of interest. Implant survival and return to function will be

summarized using a Kaplan-Meier method and presented with rates (as percentages) and confidence intervals.

B. Sample Size

Sample size is based on a longitudinal data collection model and using survivability as the primary endpoint of interest. The attrition rate is assumed to be 10%.

XII. References

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Guideline Reference:

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