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TITLE: Evaluation of a Novel Dual Antifibrotic and Proregenerative Strategy to Facilitate Improved Functional Outcomes in the Treatment of Volumetric Muscle Loss

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CONTRACTING ORGANIZATION: The Henry M. Jackson Foundation for the Advancement of Military Medicine Inc, Bethesda, MD

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14. ABSTRACT

The overall objective of the proposed work is to evaluate the safety and efficacy of administration of mCAR513 for: (1) mitigating the fibrotic wound healing response to volumetric muscle loss (VML), and (2) to enhance the efficacy of leading, near term regenerative therapies in promoting reconstitution of skeletal muscle volume and end-organ neuro-musculoskeletal function following VML injury thereby facilitating improved outcomes, namely sustained readiness and lethality of the fighting force. During this reporting period, we encountered unexpected issues in accessing mCAR513 due to supply chain issues as a result of the COVID-19 pandemic. In response, we are pursuing alternative options, to include mBMF164 as the antifibrotic intervention for this proposal. These studies have been concluded. We have included these study findings in this report.

15. SUBJECT TERMS
None listed.

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TABLE OF CONTENTS

1. INTRODUCTION:

Primary Goal & Overarching Hypothesis:

An overarching objective of our research program is to develop individualized, patient-specific (i.e., personalized medicine) therapies capable of providing the highest level of functional performance and optimal QoL for SMs and veterans with traumatic extremity injuries. However, before this can be achieved, numerous aspects of those injuries, including VML injuries, require further investigation. Thus, pre-clinical studies involving a dual anti-fibrotic and pro-regenerative therapeutic, which seek to elucidate these key questions, particularly those, focused on VML injuries, are crucial to understanding the fundamental mechanisms related to the interplay between anti-fibrosis and tissue regeneration.

The primary goal of this study is to develop a dual anti-fibrotic and pro-regenerative treatment strategy, which facilitates optimal functional outcomes following VML injury. The proposed work seeks to evaluate the safety and efficacy of administration of mCAR513 for: (1) mitigating the fibrotic wound healing response to volumetric muscle loss (VML), and (2) to enhance the efficacy of leading, near-term regenerative therapies in promoting reconstitution of skeletal muscle volume and end-organ neuro-musculoskeletal function following VML injury thereby facilitating improved outcomes, namely sustained readiness and lethality of the fighting force.

2. KEYWORDS:

Volumetric Muscle Loss, Antifibrotic, Regenerative Therapy, Skeletal Muscle, Wound Healing

3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**
    - Specific Aim 1: The *objective* of this aim is to determine if mCAR513 will enhance the efficacy with which regenerative medicine therapies mediate regeneration and functional restoration of a VML affected muscle. The *hypothesis* to be tested in this aim is that mCAR513 will promote an anti-fibrotic microenvironment within the VML wound bed thereby enhancing the efficacy regenerative medicine therapies resulting in a greater density of contractile tissue and improvements in functional capacity
    - Specific Aim 2: The objective of this aim is to determine the efficacy of a dual treatment strategy within the more challenging large animal model. The hypothesis to be tested in this aim is that an optimized dual treatment strategy will facilitate improved functional outcomes compared to either treatment in isolation. We will test this hypothesis using an established DoD relevant, large animal (porcine) model of VML with a well characterized fibrotic wound healing response that results in extensive collagen deposition that is representative of the human condition to evaluate functional outcomes following an optimized treatment strategy.

	Timeline	USUHS	Status
Specific Aim I: Characterize the spatiotemporal dynamics of skeletal muscle wound healing associated with administration of mCAR513 as an adjunct anti-fibrotic therapy to regenerative medicine treatment strategies for volumetric muscle loss.			
Sub-Aim 1A: Assess the ability of mCAR513 to dampen the fibrotic pathobiology associated with VML	**Months**	**POC**	**--**
Subtask 1A-1: Obtain IACUC & ACURO Approvals	1-3	Dearth	**Complete**
Subtask 1A-2: Perform Rodent Surgeries	3-12	Dearth / Goldman	**Ongoing**
Subtask: 1A-3: Perform In-vivo Functional Analyses	3-13	Dearth / Goldman	**Ongoing**
Subtask 1A-4: Perform Cellular, Molecular, & Histological Analyses	4-15	Dearth / Goldman	**Ongoing**
Subtask 1A-5: Data Reduction, Interpretation & Dissemination	6-16	Dearth / Goldman	**Ongoing**

Sub-Aim 1B: Evaluate the ability of mCAR513 to enhance the efficacy with which regenerative medicine therapies facilitate restoration of skeletal muscle form and function following VML	**Months**	**POC**	**--**
Subtask 1B-1: Obtain IACUC & ACURO Approvals	1-3	Dearth	**Complete**
Subtask 1B-2: Perform Rodent Surgeries	15-22	Dearth / Goldman	**Pending**
Subtask 1B-3: Perform In-vivo Functional Analyses	15-23	Dearth / Goldman	**Pending**
Subtask 1B-4: Perform Cellular, Molecular, & Histological Analyses	16-25	Dearth / Goldman	**Pending**
Subtask 4: Data Reduction, Interpretation & Dissemination	17-26	Dearth / Goldman	**Pending**
Milestone(s) Achieved: Determination of an optimized treatment strategy, consisting of an anti-fibrotic and pro-regenerative materials, which facilitates improved outcomes following VML injury.			

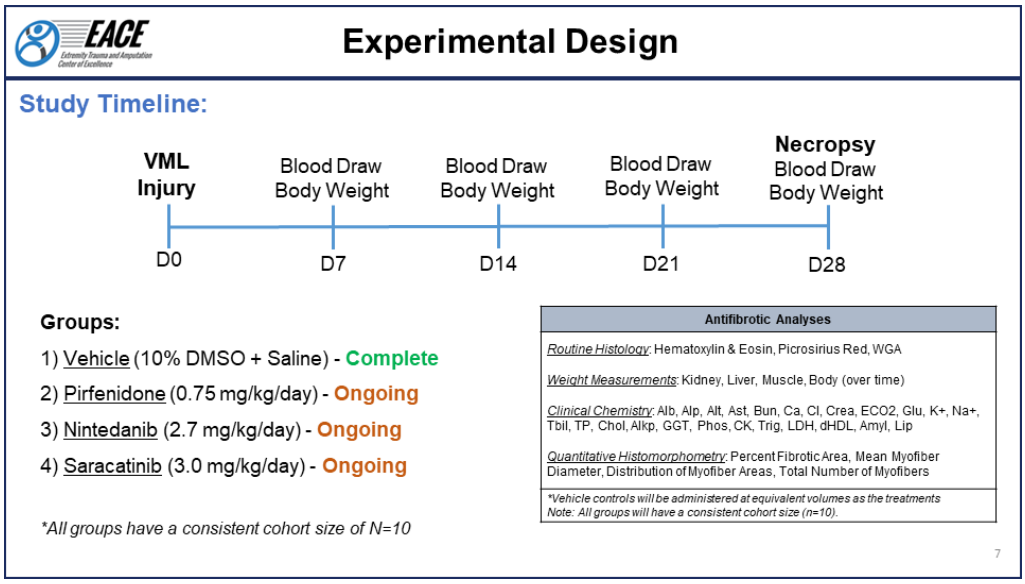
	Timeline	USUHS	Status
Specific Aim II: To characterize the ability of an optimized dual anti-fibrotic & pro-regenerative strategy to facilitate improved functional outcomes within a clinically relevant, large animal model of volumetric muscle loss			
Subtask 2-1: Obtain IACUC & ACURO Approvals	14-17	Dearth	**Complete**
Subtask 2-2: Perform Porcine Surgeries	25-30	Dearth / Goldman	**Ongoing**
Subtask 2-3: Perform In-vivo Functional Analyses	25-31	Dearth / Goldman	**Ongoing**
Subtask 2-4: Perform Cellular, Molecular, & Histological Analyses	28-35	Dearth / Goldman	**Ongoing**
Subtask 2-5: Data Reduction, Interpretation & Dissemination	30-36	Dearth / Goldman	**Ongoing**
Milestone(s) Achieved: Evaluation of the efficacy of an optimized combination therapy at facilitating the highest level of function following VML injury in a large animal model.			

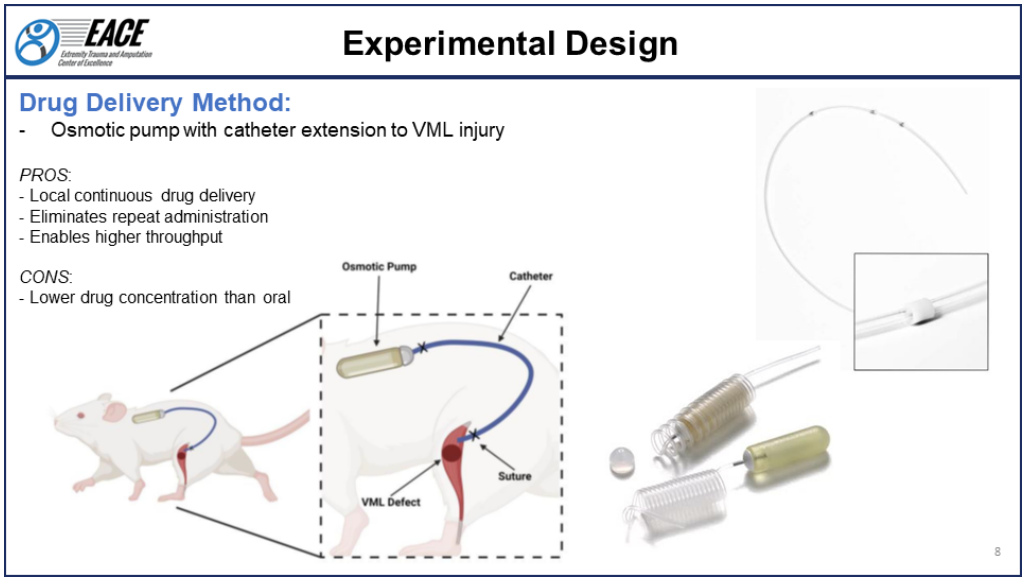
- **What was accomplished under these goals?**

  *Summary of activities/findings during the **prior** reporting cycle (**Yr1** of award):*

  As described within the prior annual report, during the initial year of the award, the investigative team devoted significant effort towards activities related to project initiation (e.g., award set up, regulatory approval, supply ordering, etc.), and initial scientific experiments. Notably, as we reported previously, the investigative team had not been able to successfully contact the CALIBR/SCRIPPS team, despite

numerous outreach efforts, and thus was unable to acquire the mCAR513 material as previously anticipated/proposed. Thus, activities were undertaken to identify potential alternative anti-fibrotic interventions. Furthermore, a series of experiments were undertaken in which these interventions were delivered via a quasi-local administration strategy. See the information within the slides below for a recap of the experimental design and delivery mechanism undertaken in those prior experiments.

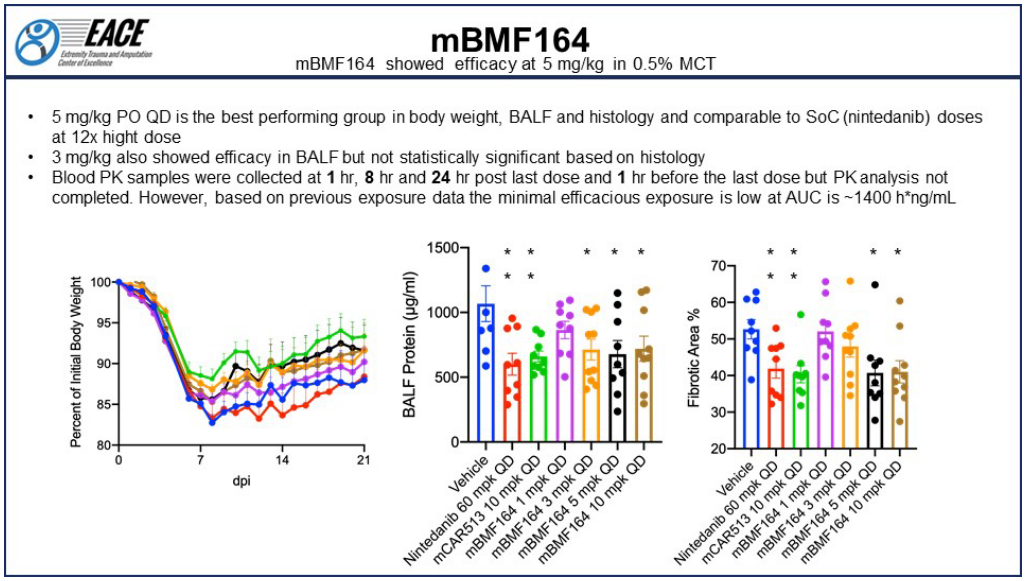




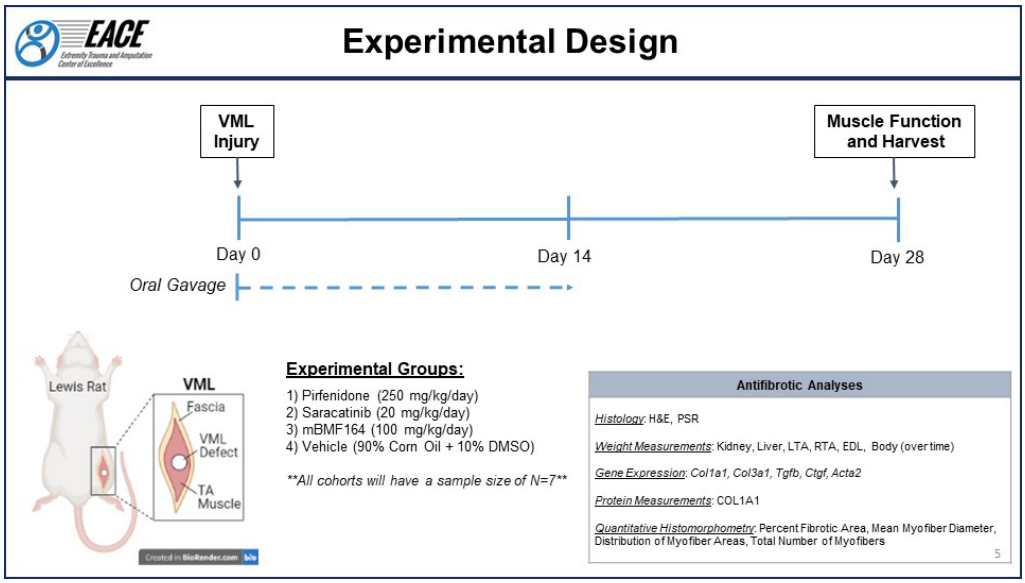
*Summary of activities/findings during the **current** reporting cycle (**Yr2** of award):*

The outcome of the initial pilot experiments described above demonstrated that the quasi-local delivery method, as potentially beneficial as it conceptually is, was challenged with technical limitations and ultimately unable to provide a standardized and consistent delivery mechanism to evaluate the study interventions. To overcome this methodological challenge, the investigative team decided to *pivot the administration mechanism to oral delivery* – i.e., via oral gavage. While this mechanism has practical considerations/downsides (e.g., very time/labor intensive to perform on a large volume of animals, etc.), it represents a classic, and potentially clinically relevant, delivery mechanism which has been well characterized previously.

Notably, since the submission of the prior annual report, *our investigative team was able to re-establish contact with the CALIBR/SCRIPPS team.* As a result of these renewed discussions, the CALIBR/SCRIPPS team informed the investigative team that there had been continued development at CALIBR/SCRIPPS on the mCAR513 compound (relative to the time of the grant proposal submission) and that they have completed a comprehensive evaluation of a new derivative compound – mBMF164. This new compound – mBMF164 – has been found to be more effective that mCAR513 (see data from the CALIBR/SCRIPPS team below), and thus, the investigative team believes that efforts within the current award should *pivot towards the use of this new, more effective compound, mBMF164*. Importantly, the intent of the award remains completed unchanged given that the new investigative agent, mBMF164, is a derivative of the originally proposed compound, mCAR513, and thus the scientific underpinning under investigation and the information/knowledge gleaned remains the same.



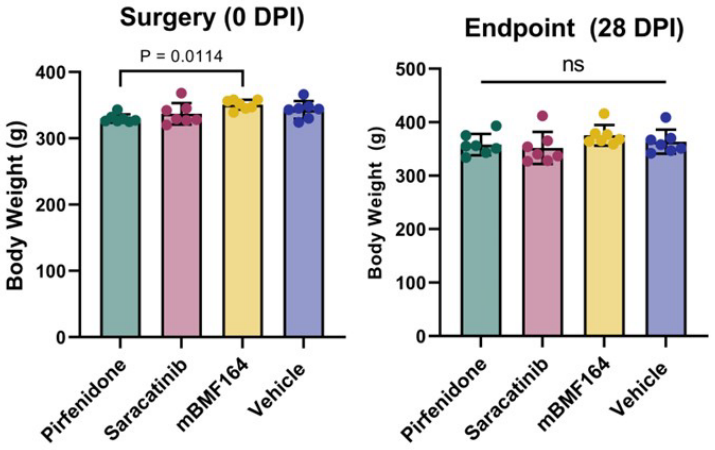
Given the availability of mBMF164, the study design for subsequent experiments was adjusted to include it as the primary intervention under investigation, in addition to the two additional investigated interventions previously noted/investigated (i.e., pirfenidone & sarcatinib), as well as an experimental control (i.e., vehicle). All experimental agents were provided for 14d via oral gavage. Muscle function remained as the primary outcome measure, in addition to a number of secondary outcome measures. See the slide below for more detail related to the study design, timelines, and outcome measures. Data/findings from those primary and secondary outcome analyses follow in the subsequent slides.



Body, Muscle, and Organ Weights

6

Body, Muscle, and Organ Weights

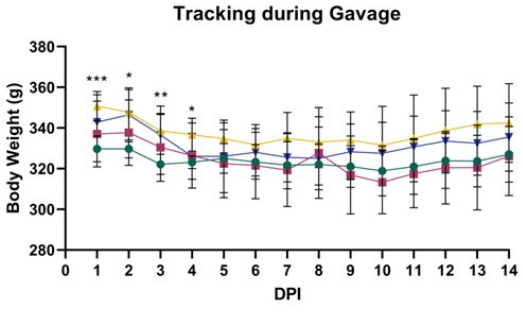


Starting difference between **PFD** and **SRC <u>surgery weights.</u>**

No difference by the study **<u>endpoint</u>**.

7

Body, Muscle, and Organ Weights



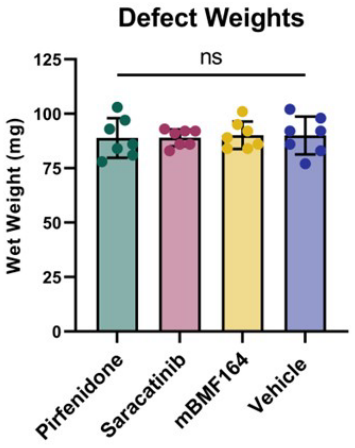
Source of Variation	% of total variation	P value
Time x Treatment	2.67	0.145
Time	10.6	<0.001
Treatment	14.0	0.140
Subject	55.8	<0.001

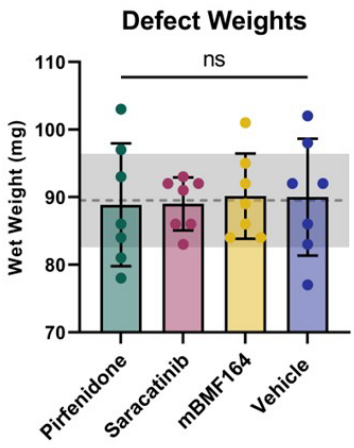
<u>No main effect</u> by **<u>treatment</u>**. Differences between PFD and mBMF164 are noted in the graph.

<u>Main effect</u> by **time** and **subject** is expected.

8

Body, Muscle, and Organ Weights



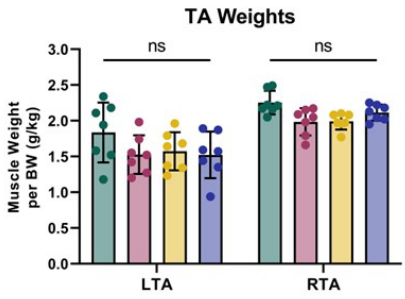


No differences in defect weights across groups.

Average = 89.5 mg
SD = 6.90

9

Body, Muscle, and Organ Weights



Main effect by **limb**.

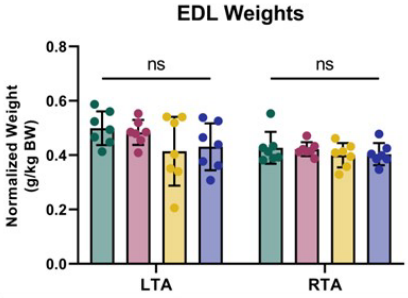
Almost **main effect** by **treatment.**
PFD is trending higher than the other groups in LTA.

Source of Variation	% of total variation	P value	P value summary
Limb x Treatment	1.02	0.679	ns
Limb	44.3	<0.001	****
Treatment	10.5	0.051	ns
Subject	28.1	0.087	ns

Holm-Šídák's multiple comparisons test	Adjusted P Value
LTA	
Pirfenidone vs. Saracatinib	0.140
Pirfenidone vs. mBMF164	0.214
Pirfenidone vs. Vehicle	0.140
Saracatinib vs. mBMF164	0.975
Saracatinib vs. Vehicle	0.975
mBMF164 vs. Vehicle	0.975
RTA	
Pirfenidone vs. Saracatinib	0.281
Pirfenidone vs. mBMF164	0.281
Pirfenidone vs. Vehicle	0.770
Saracatinib vs. mBMF164	0.967
Saracatinib vs. Vehicle	0.770
mBMF164 vs. Vehicle	0.770

10

Body, Muscle, and Organ Weights



Main effect by **limb**, Left EDLs are larger than Right EDLs.

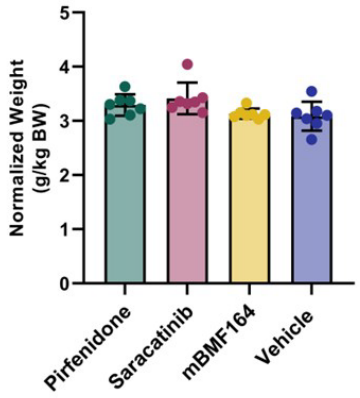
Source of Variation	% of total variation	P value	P value summary
limb x treatment	2.74	0.654	ns
limb	9.33	0.026	*
treatment	10.7	0.105	ns
Subject	37.4	0.562	ns

Holm-Šídák's multiple comparisons test	Adjusted P Value
LTA	
Pirfenidone vs. Saracatinib	0.880
Pirfenidone vs. mBMF164	0.138
Pirfenidone vs. Vehicle	0.276
Saracatinib vs. mBMF164	0.276
Saracatinib vs. Vehicle	0.390
mBMF164 vs. Vehicle	0.880
RTA	
Pirfenidone vs. Saracatinib	0.988
Pirfenidone vs. mBMF164	0.975
Pirfenidone vs. Vehicle	0.975
Saracatinib vs. mBMF164	0.975
Saracatinib vs. Vehicle	0.975
mBMF164 vs. Vehicle	0.988

11

Body, Muscle, and Organ Weights

Left Kidney



Significant differences between groups.

SRC** and **PFD** are **heavier than mBMF and VEH groups.

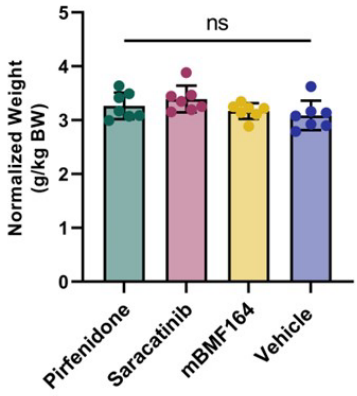
Kruskal-Wallis test	
P value	0.0279
Exact or approximate P value?	Approximate
P value summary	*
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	4
Kruskal-Wallis statistic	9.11

Dunn's multiple comparisons test	Adjusted P Value
Pirfenidone vs. Saracatinib	>0.9999
Pirfenidone vs. mBMF164	0.7132
Pirfenidone vs. Vehicle	0.5468
Saracatinib vs. mBMF164	0.0972
Saracatinib vs. Vehicle	0.0676
mBMF164 vs. Vehicle	>0.9999

12

Body, Muscle, and Organ Weights

Right Kidney



No differences between **right kidney** weights.

SRC is trending heavier than VEH, not significant.

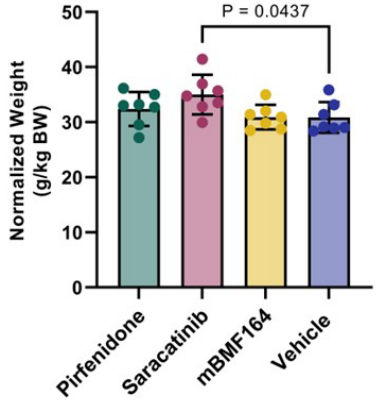
ANOVA summary	
F	2.21
P value	0.1128
P value summary	ns
Significant diff. among means (P < 0.05)?	No
R squared	0.217

Holm-Šídák's multiple comparisons test	Adjusted P Value
Vehicle vs. Pirfenidone	0.2983
Vehicle vs. Saracatinib	0.0657
Vehicle vs. mBMF164	0.5183

13

Body, Muscle, and Organ Weights

Liver



Significant differences between **liver** weights.

SRC liver weight is ***heavier*** than VEH.

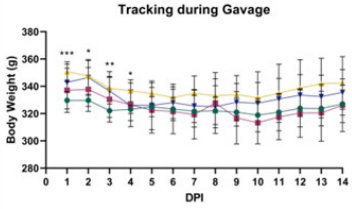
ANOVA summary	
F	3.02
P value	0.0495
P value summary	*
Significant diff. among means (P < 0.05)?	Yes
R squared	0.274

Holm-Šídák's multiple comparisons test	Adjusted P Value
Vehicle vs. Pirfenidone	0.5603
Vehicle vs. Saracatinib	0.0437
Vehicle vs. mBMF164	0.9642

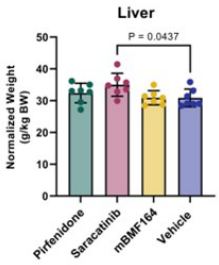
14

Conclusions

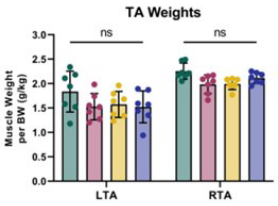
1) No differences in body weights during gavage treatment.



2) Saracatinib has a negative effect on organ weights.



3) Pirfenidone appears to have a positive effect on muscle weights.



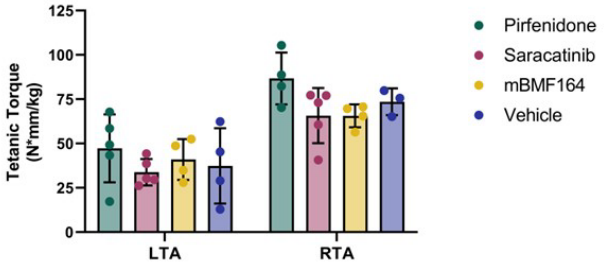
*** Starting weights were not heavier than other groups. Nor were defect weights lower than other groups. ***

15

Muscle Function

16

Muscle Function (Norm to BW)

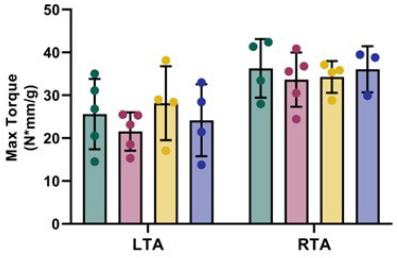


No differences between treatment groups for injured (LTA) limbs.

Fixed effects (type III)	P value	P value summary
limb	<0.001	****
treatment	0.083	ns
limb x treatment	0.743	ns

17

Muscle Function (Norm to TA)



- Pirfenidone
- Saracatinib
- mBMF164
- Vehicle

No differences in muscle function when normalized to *TA weights*.

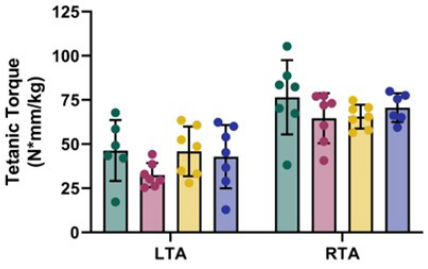
Elevated function in Pirfenidone treatment group goes down with TA weight normalization.

Fixed effects (type III)	P value	P value summary
limb	<0.001	***
treat	0.644	ns
limb x treat	0.790	ns

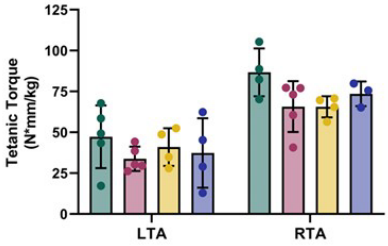
18

Conclusions

1) **No differences between treatments for max torque.**



2) **With bad curves removed, still no differences between treatments for max torque.**

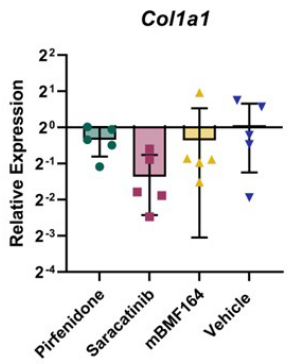


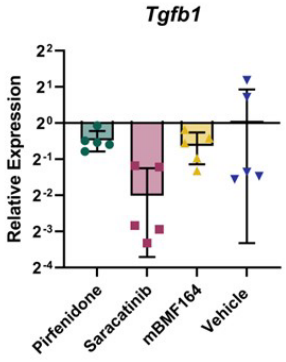
19

Molecular Analysis:
qPCR & ELISA

20

qPCR Analysis

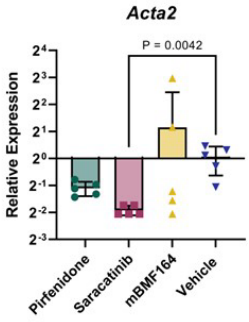


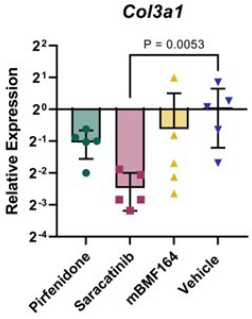


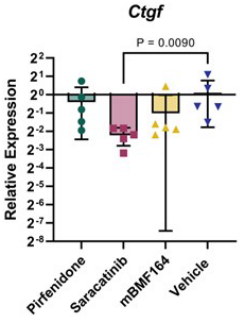
No differences in Col1a1 or TGFb1 expression.

21

qPCR Analysis







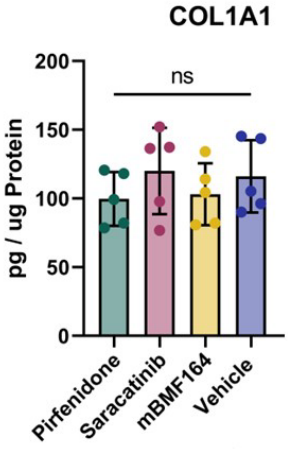
SRC treatment results in significantly **less expression of *Acta2*** compared to VEH.

SRC treatment results in significantly **less expression of *Ctgf*** compared to VEH.

SRC treatment results in significantly **less expression of *Ctgf*** compared to VEH.

22

Protein Analysis

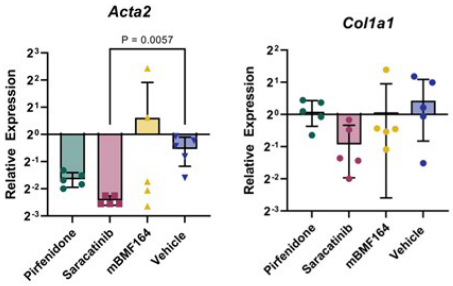


No differences in COL1A1 muscle tissue protein levels between treatment groups.

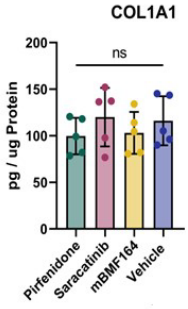
23

Conclusions

1) Saracatinib treatment results in *decreased* expression of *Acta2*, *Col3a1*, and *Ctgf* by 28 DPI.



2) *No differences* between treatments in COL1A1 protein in the injured limbs by 28 DPI.



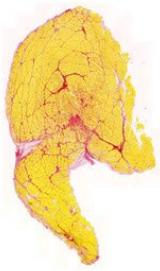
24

Histology Assessment:
PSR & HE

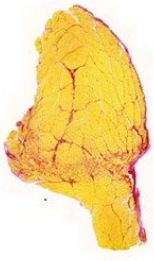
25

PSR Qualitative Analysis

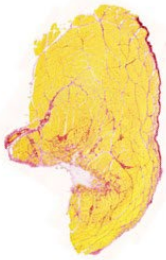
Vehicle - Control



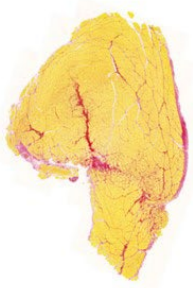
Pirfenidone



Saracatinib

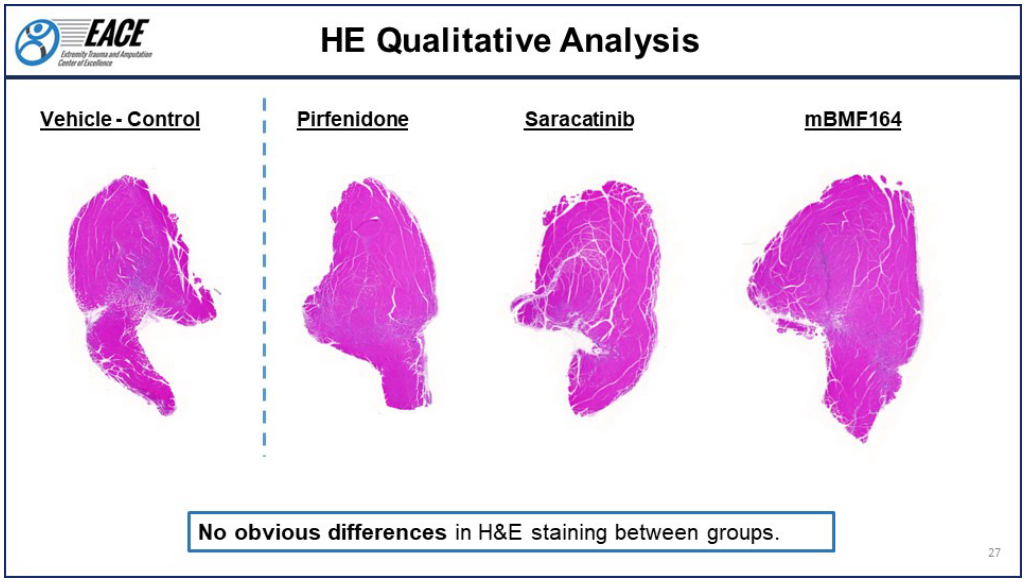


mBMF164



No obvious differences in collagen staining between groups.

26

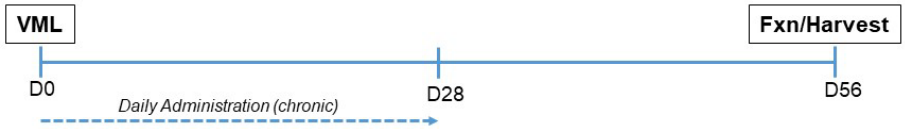


In summary, the totality of the data presented above suggest the following conclusions:

- Effect on overall animal health
  - No differences were observed in animal body weight during the gavage treatment timeline (14 days) between any of the interventions
  - Saracatinib treatment was shown to elicit a decrease in organ weight following the experimental timeline
  - Pirfenidone treatment was shown to increase muscle weight
- Effect on muscle function
  - No differences were observed in max torque at the end of the experimental timeline between any of the interventions
- Effect on muscle biology/physiology
  - Saracatinib treatment results in decreased expression of several fibrotic genes at 28 days.
  - The differences in gene expression were not observed in protein expression as there were no differences in COL1A1 protein expression across treatment groups at 28 days.

Next, the team sought to undertake experiments aimed at optimizing the dosing of the primary experimental intervention – mBMF164. Three doses of mBMF164 (low, medium, high), as well as an experimental control (i.e., vehicle), were evaluated out to a 56d timepoint. This timepoint was chose due to the documented extensive fibrosis found at this timepoint following VML injury. All does were provided for 28d via oral gavage. Muscle function remained as the primary outcome measure, in addition to a number of secondary outcome measures. See the slide below for more detail related to the study design, timelines, and outcome measures. Data/findings from those primary and secondary outcome analyses follow in the subsequent slides.

Experimental Design: mBMF164 Dosing



Treatment	Daily Dose	Cohort Size
mBMF164 – High	20 mg/kg	N = 10
mBMF164 – Medium	10 mg/kg	N = 10
mBMF164 – Low	5 mg/kg	N = 10
Vehicle Control	Equal Vol.	N = 10
Optional:		
Pirfenidone	250 mg/kg	N = 10
Total Animals = 40 + 10 optional		

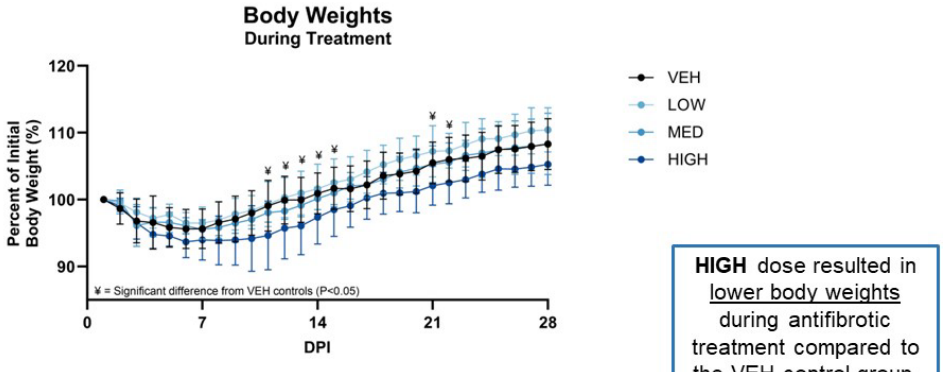
Antifibrotic Analyses
Histology: H&E, PSR, WGA
Weight Measurements: Kidney, Liver, LTA, RTA, EDL, Body (over time)
Gene Expression: Col1a1, Col3a1, Tgfb, Ctgf, Acta2
Protein Measurements: Hydroxyproline, COL1A1, TGFB1
Quantitative Histomorphometry: Percent Fibrotic Area, Mean Myofiber Diameter, Distribution of Myofiber Areas, Total Number of Myofibers

30

Body & Muscle Weights

33

Body Weights During Treatment

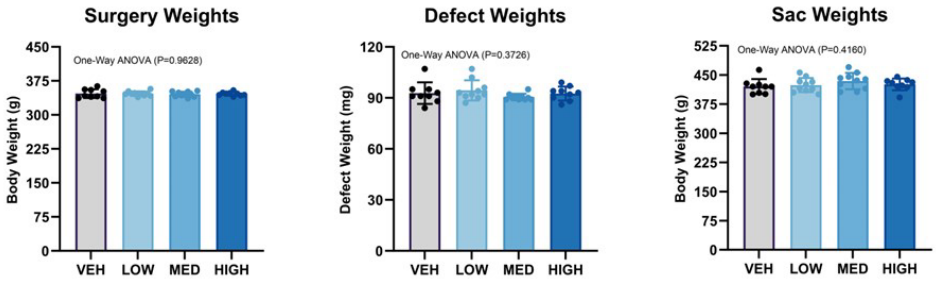


Fixed effects (type III)	P value	P value summary
Time	<0.0001	****
Treatment	0.0136	*
Time x Treatment	0.0004	***

HIGH dose resulted in lower body weights during antifibrotic treatment compared to the VEH control group.

34

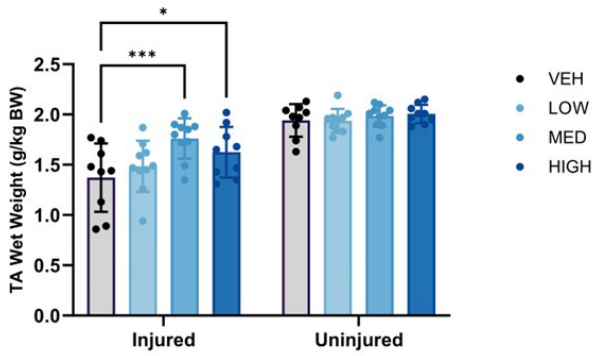
Surgery, Sac, Defect Weights



No differences in body weights at surgery or study endpoint. Likewise, defect weights were no different across all groups.

35

TA Weights (Norm to BW)



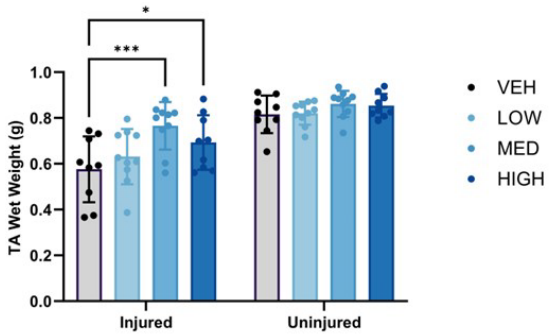
MED and **HIGH** dose resulted in *heavier TA* wet weights compared to VEH controls.

No differences were observed for the uninjured TA weights.

Source of Variation	% of total variation	P value	P value summary	Significant?
Limb x Treatment	4.383	0.0443	*	Yes
Limb	46.10	<0.0001	****	Yes
Treatment	7.983	0.0250	*	Yes
Subject	25.64	0.1046	ns	No

36

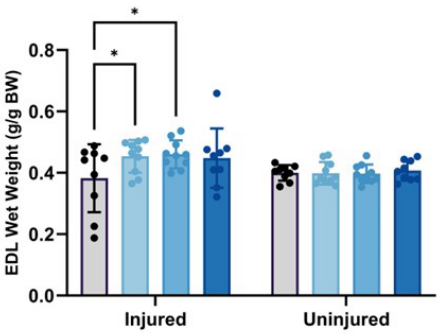
TA Weights (Raw Data)



Source of Variation	% of total variation	P value	P value summary
Limb x Treatment	3.711	0.0429	*
Limb	40.09	<0.0001	****
Treatment	11.09	0.0161	*
Subject	31.81	0.0091	**

37

EDL Weights (Norm to BW)



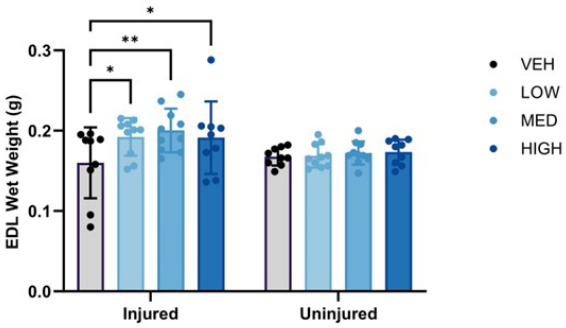
Source of Variation	% of total variation	P value	P value summary
Limb x Treatment	5.839	0.1644	ns
Limb	7.657	0.0117	*
Treatment	5.823	0.2276	ns
Subject	43.49	0.3095	ns

LOW and **MED** dose resulted in *heavier EDL* wet weights compared to VEH controls.

No differences were observed for the uninjured TA weights.

38

EDL Weights (Raw Data)



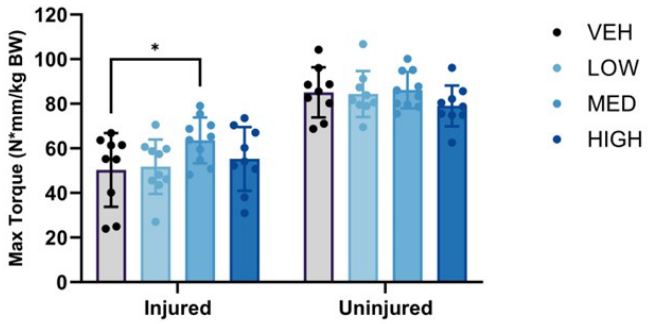
Source of Variation	% of total variation	P value	P value summary
Limb x Treatment	5.581	0.1451	ns
Limb	7.065	0.0107	*
Treatment	8.497	0.1155	ns
Subject	45.37	0.1781	ns

39

Neuromuscular Functional Assessment

40

Muscle Function (Norm to BW)



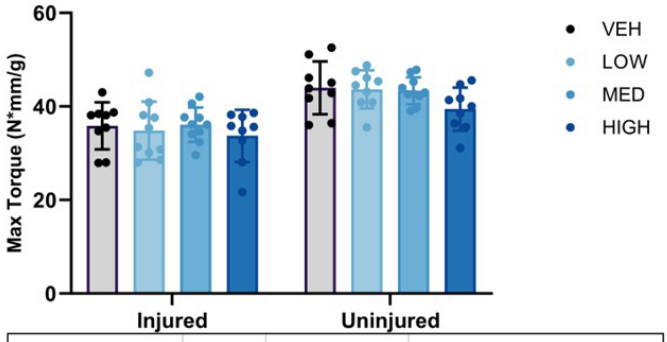
MED dose resulted in *higher muscle function* compared to VEH controls.

No differences were observed for the uninjured TA weights.

Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?
Limb	<0.0001	****	Yes
Treatment	0.2745	ns	No
Limb x Treatment	0.1169	ns	No

41

Muscle Function (Norm to TA)



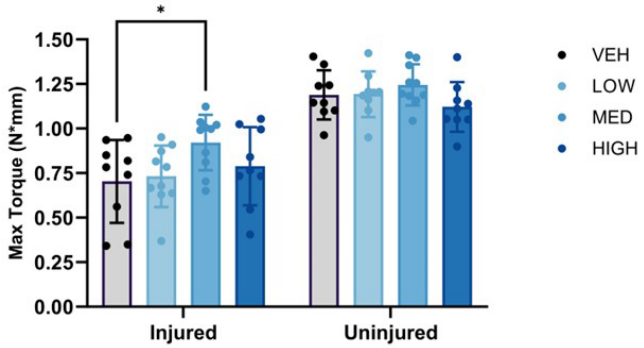
No differences between injured limb muscle function when normalized to TA weights.

No differences were observed for the uninjured TA weights.

Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?
Limb	<0.0001	****	Yes
Treatment	0.2717	ns	No
Limb x Treatment	0.5972	ns	No

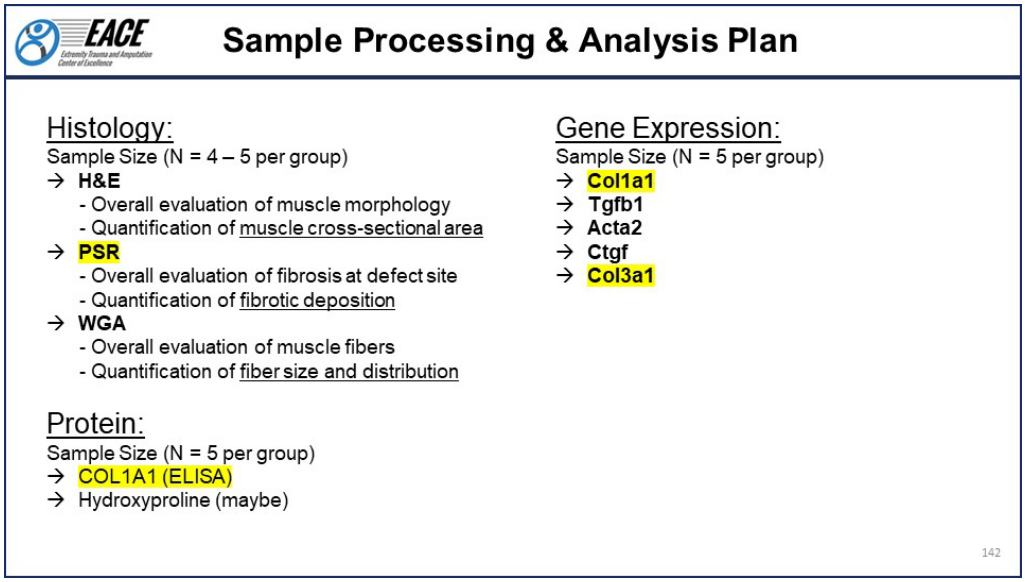
42

Muscle Function (Raw Data)



Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?
Limb	<0.0001	****	Yes
Treatment	0.1237	ns	No
Limb x Treatment	0.1218	ns	No

43



- **What opportunities for training and professional development has the project provided?**

  Nothing to report

- **How were the results disseminated to communities of interest?**

  Nothing to report

- **What do you plan to do during the next reporting period to accomplish the goals?**
    - During the next reporting period, we plan to accomplish the items listed below:
        - Continue to assess mBMF164 as an antifibrotic treatment for VML injuries
        - Complete Subtask 1A-1 through Subtask 1A-5 of Specific Aim 1
        - Begin Subtask 1B-1 through Subtask 1B-5 of Specific Aim 1
        - Continue Specific Aim 2

4. IMPACT

- **What was the impact on the development of the principal discipline(s) of the project?**

  Nothing to report

- **What was the impact on other disciplines?**

  Nothing to report

- **What was the impact on technology transfer?**

  Nothing to report

- **What was the impact on society beyond science and technology?**

  Nothing to report.

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change:**

  We have completed our alternative antifibrotic evaluation studies (including pirfenidone, Nintedanib, saracatinib, mBMF164). Due to the results from the pilot study, we have chosen to pursue mBMF164 as the choice alternative to mCAR513 for the following reasons: (1) mBMF164 is chemically closely related to mCAR513, and (2) mBMF164 was developed by the same research group (CALIBR) as mCAR513.

- **Actual problems or delays and actions to resolve them:**

  Nothing to report.

- **Anticipated Problems/Issues**

  Assuming there are no additional COVID-19 associated restrictions/supply chain issues, and/or any additional unexpected scientific outcomes, we do not anticipate any additional problems/issues for this project.

- **Changes that had a significant impact on expenditures:**

  Nothing to report

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents:**

  We have changed the route of delivery for the antifibrotic from subcutaneous pumps to daily oral gavage. As such, we have updated the IACUC protocol to reflect these changes.

6. PRODUCTS:

- **Publications, conference papers, and presentations:**

  Poster Presentation at Military Health Services Research Symposium 2023

- **Website(s) or other Internet site(s):**

  Nothing to Report

- **Technologies or techniques:**

  Nothing to Report

- **Inventions, patent applications, and/or licenses:**

  Nothing to Report

- **Other Products:**

  Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

Name:	Christopher L. Dearth, PhD
Project Role:	Principal Investigator
Nearest person month worked:	1
Contribution to project:	Dr. Dearth led the coordination of all aspects of the project related activities, including: budgetary management, personnel management, regulatory (IACUC) approvals, and experimental/laboratory activities, among others.
Name:	Stephen M. Goldman, PhD
Project Role:	Co-Investigator
Nearest person month worked:	1
Contribution to project:	Dr. Goldman assisted Dr. Dearth with project related activities, including: personnel management, regulatory (IACUC) approvals, and experimental/laboratory activities.
Name:	Jessica M. Motherwell, PhD
Project Role:	Co-Investigator
Nearest person month worked:	1
Contribution to project:	Dr. Motherwell assisted Dr. Dearth with project related activities, including: regulatory (IACUC) approvals, and experimental/laboratory activities.
Name:	Claudia Hernandez
Project Role:	Veterinary Technician
Nearest person month worked:	4.4
Contribution to project:	Ms. Hernandez assisted with project related experimental activities.
Name:	Ondine Eken
Project Role:	Research Assistant III
Nearest person month worked:	0.55
Contribution to project:	Ms. Eken assisted with project related experimental activities.
Name:	Heidi Mahatan
Project Role:	Program Manager
Nearest person month worked:	0.10
Contribution to project:	Ms. Mahatan assisted with project management related activities, including: budget management, approval of supply purchases, and hiring actions and staff supervision.
***Note: Drs. Dearth, Goldman & Motherwell are GS DoD employees (part of the EACE), thus their efforts are at no cost to the award.	

- **Has there been a change in active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

  Nothing to report

- **What other organizations were involved as partners?**

  Nothing to report

8. SPECIAL REPORTING REQUIREMENTS:

- **COLLABORATIVE AWARDS:**

  Nothing to report

- **QUAD CHARTS:**

  Nothing to report

9. APPENDICES:

N/A