TABLE OF CONTENTS

LIST OF TABLES

3.2.P.8.3. STABILITY DATA – THERMAL – STRESS AND CYCLING

Data from stability studies on BNT162b2 drug product lots stored at the thermal stress conditions of 25 ± 2 °C/60 ± 5% RH and 30 ± 2 °C/65 ± 5% RH, as well as thermal cycling studies, are presented for emergency supply and process performance qualification lots manufactured by Polymun Scientific (with fill and finish at Pfizer, Puurs), mibe (with fill and finish at Pfizer, Puurs), Pfizer, Puurs and Pfizer, Kalamazoo, MI.

Additionally, data from supportive stability studies for one clinical BNT162b2 drug product lot stored at the thermal stress condition of 25 ± 2 °C and manufactured by Polymun Scientific is also presented.

All studies are listed in Table 3.2.P.8.3-1. Results will be provided in Table 3.2.P.8.3-2 through Table 3.2.P.8.3-22.

Table 3.2.P.8.3-1. Summary of Drug Product Thermal Stability Studies

Lot Number	Drug Product Batch Use	Stability Start Date	Study Type	Storage Condition	Stability Data Presented	Data Table Location
EL8723 (Pfizer, Puurs)	Stability, Clinical, Emergency Supply[a], Process performance qualification	January 2021	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-2
			Thermal Stress	30 ± 2 °C/65 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-3
		(TC Study: February 2021)	Thermal Cycling: Ultra frozen vials are placed at -20 ± 5 °C for 4 weeks and then moved to 2 to 8°C for 12 weeks. Samples will be pulled for testing every 2 weeks throughout protocol.		8 weeks (On-going)	Table 3.2.P.8.3-19
EL3248 (Pfizer, Kalamazoo, Line (a))	Stability, Clinical, Emergency Supply[a], Process performance qualification	December 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-4
			Thermal Stress	30 ± 2 °C/65 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-5
EN1195 (mibe/Pfizer, Puurs)	Stability, Emergency Supply[a], Process performance qualification	February 2021	Thermal Cycling: Ultra frozen vials are placed at -20 ± 5 °C for 4 weeks and then moved to 2 to 8°C for 12 weeks. Samples will be pulled for testing every 2 weeks throughout protocol.		6 weeks (On-going)	Table 3.2.P.8.3-17
EL9266 (Pfizer, Kalamazoo, Line (b))	Stability, Emergency Supply[a], Process performance qualification	February 2021	Thermal Cycling: Ultra frozen vials are placed at -20 ± 5 °C for 4 weeks and then moved to 2 to 8°C for 12 weeks. Samples will be pulled for testing every 2 weeks throughout protocol.		8 weeks (On-going)	Table 3.2.P.8.3-18
EL3249 (Pfizer, Kalamazoo, Line (b))	Stability, Clinical, Emergency Supply[a], Process performance qualification	January 2021	Thermal Cycling: 1 week at -90 to -60°C , followed by 2 weeks at -20 ± 5 °C, 4 weeks at 2 to 8°C and 1 week at 25 ± 2 °C/60 ± 5% RH.		8 weeks (Complete)	Table 3.2.P.8.3-20
EK4242 (mibe/Pfizer, Puurs)	Stability, Emergency Supply[a], Process performance qualification	January 2021	Thermal Cycling: 1 week at -90 to -60°C followed by 4 weeks at 2 to 8°C		5 weeks (Complete)	Table 3.2.P.8.3-21
EL7834 (Polymun Scientific/Pfizer, Puurs	Stability, Emergency Supply[a], Process performance qualification	January 2021	Thermal Cycling: 1 week at -90 to -60°C followed by 4 weeks at -20 ± 5 °C and then 4 weeks at 2 to 8°C. and 1 week at 25 ± 2 °C/60 ± 5% RH.		10 weeks (Complete)	Table 3.2.P.8.3-22

Table 3.2.P.8.3-1. Summary of Drug Product Thermal Stability Studies

Lot Number	Drug Product Batch Use	Stability Start Date	Study Type	Storage Condition	Stability Data Presented	Data Table Location
EH9899 Pfizer, Kalamazoo)	Stability, Emergency Supply[a]	November 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-6
EJ1688 (mibe/Pfizer, Puurs)	Stability, Emergency Supply[a]	November 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-7
EK1768 (Polymun Scientific/Pfizer, Puurs	Stability, Emergency Supply[a], Clinical inventory	November 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-8
			Thermal Cycling: 2 weeks at -90 to -60°C followed by 4 weeks at -20 ± 5 °C and then 8 weeks at 2 to 8°C. Samples will be pulled for testing every 2 weeks throughout protocol.		14 weeks (Complete)	Table 3.2.P.8.3-15
EJ1686 (Polymun Scientific/Pfizer, Puurs	Stability, Emergency Supply[a], Clinical inventory	November 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-9
			Thermal Cycling: 2 weeks at -90 to -60°C followed by 4 weeks at -20 ± 5 °C and then 8 weeks at 2 to 8°C. Samples will be pulled for testing every 2 weeks throughout protocol.		14 weeks (Complete)	Table 3.2.P.8.3-16
EJ1685 (Polymun Scientific/Pfizer, Puurs	Stability, Emergency Supply[a], Clinical inventory	November 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-10
EJ0553 (Polymun Scientific/Pfizer, Puurs	Stability, Emergency Supply[a], Clinical inventory	November 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-11
EE8493 (Polymun Scientific/Pfizer, Puurs)	Stability, Emergency Supply[a], Clinical inventory	September 2020	Thermal Stress	25 ± 2 °C/60 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-12
			Thermal Stress	30 ± 2 °C/65 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-13
BCV40420-A (Polymun Scientific)	Stability, Clinical	May 2020	Thermal Stress	25 ± 2 °C	4 months (complete)	Table 3.2.P.8.3-14

a. Emergency supply designation applies to US market.
b. A minimum of one PPQ lot will be enrolled in thermal stress and thermal cycling stability programs compliant with ICH Guidelines and further information on lot numbers, manufacture, stability enrollment and available data will be provided in the future.
TBD = To Be Determined

Table 3.2.P.8.3-2. Stability Data for Drug Product PPQ Lot EL8723 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0 [b]	WOS	Meets	(b) (4)				
1W	WOS	Meets					
2W	WOS	Meets					
1M	WOS	Meets					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing.
b. T=0 testing performed for this lot (release values not utilized.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-3. Stability Data for Drug Product PPQ Lot EL8723 Stored at 30 ± 2 °C/65 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0 [b]	WOS	Meets	(b) (4)				
1W	WOS	Meets					
2W	WOS	Meets					
1M	WOS	Meets					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in

b. T=0 testing performed for this lot (release values not utilized.

W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-4. Stability Data for Drug Product PPQ Lot EL3248 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	White to off-white suspension	May contain white to off-white opaque, amorphous particles	7.4 ± 0.5	(b) (4)			
0	WOS	Meets	(b) (4)				
1W	WOS	Meets					
2W	WOS	Meets					
3W	WOS	Meets					
1M	WOS	Meets					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
3W						
1M						

a. Acceptance criteria in place at time of testing.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-5. Stability Data for Drug Product PPQ Lot EL3248 Stored at 30 ± 2 °C/65 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	White to off-white suspension	May contain white to off-white opaque, amorphous particles	7.4 ± 0.5	(b) (4)			
0	WOS	Meets	(b) (4)				
1W	WOS	Meets					
2W	WOS	Meets					
3W	WOS	Meets					
1M	WOS	Meets					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
3W						
1M						

a. Acceptance criteria in place at time of testing.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-6. Stability Data for Drug Product Emergency Supply Batch EH9899 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0 [b]	White to off-white suspension	(b)	(b) (4)				
1W	White to off-white suspension	(b)					
2W	White to off-white suspension	(b)					
1M	White to off-white suspension	(b)					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 1 week time point.
b. T=0 testing performed for this lot (release values not utilized.
c. Result invalidated and not repeated as 1 month time point was pulled for testing.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-7. Stability Data for Drug Product Emergency Supply Batch EJ1688 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0	White to off-white suspension	(b)	(b) (4)				
1W	White to off-white suspension	(b)					
2W	White to off-white suspension	(b)					
1M	White to off-white suspension	Meets (b)					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 1 month time point.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-8. Stability Data for Drug Product Emergency Supply Batch EK1768 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0	White to off-white suspension	(b)	(b) (4)				
1W	White to off-white suspension	Meets (b)					
2W	White to off-white suspension	Meets (b)					
1M	White to off-white suspension	Meets (b)					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 1 week time point.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-9. Stability Data for Drug Product Emergency Supply Batch EJ1686 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0[b]	White to off-white suspension	(b)	(b) (4)				
1W	White to off-white suspension	Meets (b)					
2W	White to off-white suspension	Meets (b)					
1M	White to off-white suspension	Meets (b)					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0[b]	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 1 week time point.
b. T=0 testing performed for this lot (release values not utilized.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-10. Stability Data for Drug Product Emergency Supply Batch EJ1685 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0	White to off-white suspension	(b)	(b) (4)				
1W	White to off-white suspension	(b)					
2W	White to off-white suspension	Meets (b)					
1M	White to off-white suspension	Meets (b)					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 2 week time point.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-11. Stability Data for Drug Product Emergency Supply Batch EJ0553 Stored at 25 ± 2 °C/60 ± 5% RH

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
0	White to off-white suspension	(b)	(b) (4)				
1W	White to off-white suspension	(b)					
2W	White to off-white suspension	(b)					
1M	White to off-white suspension	(b)					

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
0	(b) (4)					
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 1 month time point.
W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; (b) (4) ; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-12. Stability Data for Drug Product EE8493 Stored at 25 ± 2 °C/60 ± 5% RH

Time	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visible)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Acceptance Criteria[a]	**White to off-white suspension**	(b)	**7.4 ± 0.5**	(b) (4)			
0	White to off-white suspension	(b)	(b) (4)				
2W	White to off-white suspension	(b)					
1M	White to off-white suspension	(b)					

Time	HPLC-CAD				Cell-based (b) (4)	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Acceptance Criteria[a]	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**% Cells Positive**	(b) (4)
0	(b) (4)					
2W						
1M						

a. Acceptance criteria in place at time of testing.
b. Original result investigated and invalidated with no result being reported.
W = Week, M = Month, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, MCR = Meets Compendial Requirements

Table 3.2.P.8.3-13. Stability Data for Drug Product EE8493 Stored at 30 ± 2 °C/65 ± 5% RH

Time	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visible)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Acceptance Criteria[a]	**White to off-white suspension**	(b)	**7.4 ± 0.5**	(b) (4)			
0	White to off-white suspension	(b)	(b) (4)				
2W	White to off-white suspension	(b)					
1M	White to off-white suspension	(b)					

Time	HPLC-CAD				Cell-based (b) (4)	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Acceptance Criteria[a]	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**% Cells Positive**	(b) (4)
0	(b) (4)					
2W						
1M						

a. Acceptance criteria in place at time of testing.
b. Original result investigated and invalidated with no result reported.
W = Week, M = Month, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, MCR = Meets Compendial Requirements

Table 3.2.P.8.3-14. Stability Data for Polymun Scientific Drug Product BNT162b2 Lot BCV40420-A Stored at 25 ± 2 °C

Time (Months)	Appearance	pH	LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Acceptance Criteria[a]	**White to off-white suspension/Free from observable particles**	**7.4 ± 0.5**	(b) (4)			
0	Pass	(b) (4)	(b) (4)			
0.5	Pass	NS				
1	Pass	NS				
2	Pass	NS				
3	Pass	(b) (4)				
4	Pass	NS				

Time (Months)	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	RNA Integrity
Acceptance Criteria[a]	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**Report Results (mg/mL)**	**Report Results (mg/mL)**	(b) (4)
0	(b) (4)				
0.5					
1					
2					
3					
4					

a. Acceptance criteria in place at time of testing.
S = Scheduled, NS = Not Scheduled at Time Point, LNP = Lipid Nanoparticle

Table 3.2.P.8.3-15. Thermal Cycling Stability Data for Drug Product Emergency Supply Batch EK1768

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -90 to -60°C (for 2 weeks)							
0	WOS	(b)	(b) (4)				
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)							
2W	WOS	Meets	(b) (4)	(b) (4)			
4W	WOS	Meets	(b) (4)				
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets	(b) (4)	(b) (4)			
8W	WOS	Meets	(b) (4)				
10W	WOS	Meets	(b)				
12W	WOS	Meets	(b) (4)				
14W	WOS	Meets	(b) (4)				

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -90 to -60°C (for 2 weeks)						
0	(b) (4)					
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)						
2W	(b) (4)					
4W						
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W	(b) (4)					
8W						
10W						
12W						
14W						

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 8 week time point.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-16. Thermal Cycling Stability Data for Drug Product Emergency Supply Batch EJ1686

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -90 to -60°C (for 2 weeks)							
0[b]	WOS	(b)	(b) (4)				
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)							
2W	WOS	Meets	(b) (4)	(b) (4)			
4W	WOS	Meets	(b) (4)				
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets	(b) (4)	(b) (4)			
8W	WOS	Meets	(b) (4)				
10W	WOS	Meets	(b) (4)				
12W	WOS	Meets	(b) (4)				
14W	WOS	Meets	(b) (4)				

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -90 to -60°C (for 2 weeks)						
0[b]	(b) (4)					
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)						
2W	(b) (4)					
4W						
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W	(b) (4)					
8W						
10W						
12W						
14W						

Table 3.2.P.8.3-16. Thermal Cycling Stability Data for Drug Product Emergency Supply Batch EJ1686

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content

a. Acceptance criteria in place at time of testing. Current effective acceptance criteria established at the 8 week time point.
b. Initial data (t0) are not from release testing. Analysis for t0 were repeated for this study.
W = Week, S = To be Scheduled, (b) (4) , LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-17. Thermal Cycling Stability Data for Drug Product PPQ Lot EN1195

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	White to off-white suspension	May contain white to off-white opaque, amorphous particles	7.4 ± 0.5	(b) (4)			
Placed @ -20 ± 5°C (for 4 weeks)							
0	WOS	Meets	(b) (4)	(b) (4)			
2W	WOS	Meets					
4W	WOS	Meets					
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets	(b) (4)	(b) (4)			
8W	S	S	S	S	S	S	S
10W	S	S	S	S	S	S	S
12W	S	S	S	S	S	S	S
14W	S	S	S	S	S	S	S
16W	S	S	S	S	S	S	S

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -20 ± 5°C (for 4 weeks)						
0	(b) (4)					
2W						
4W						
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W	(b) (4)					
8W	S	S	S	S	S	S
10W	S	S	S	S	S	S
12W	S	S	S	S	S	S
14W	S	S	S	S	S	S
16W	S	S	S	S	S	S

Table 3.2.P.8.3-17. Thermal Cycling Stability Data for Drug Product PPQ Lot EN1195

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content

a. Acceptance criteria in place at time of testing.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-18. Thermal Cycling Stability Data for Drug Product PPQ Lot EL9266

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -20 ± 5°C (for 4 weeks)							
0[b]	WOS	Meets	(b) (4)	(b) (4)			
2W	WOS	Meets					
4W	WOS	Meets					
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets	(b) (4)	(b) (4)			
8W	WOS	Meets					
10W	S	S	S	S	S	S	S
12W	S	S	S	S	S	S	S
14W	S	S	S	S	S	S	S
16W	S	S	S	S	S	S	S

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -20 ± 5°C (for 4 weeks)						
0[b]	(b) (4)					
2W						
4W						
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W	(b) (4)					
8W						
10W	S	S	S	S	S	S
12W	S	S	S	S	S	S
14W	S	S	S	S	S	S
16W	S	S	S	S	S	S

Table 3.2.P.8.3-18. Thermal Cycling Stability Data for Drug Product PPQ Lot EL9266

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content

a. Acceptance criteria in place at time of testing.
b. Initial data (t0) are not from release testing. Analysis for t0 were repeated for this study.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-19. Thermal Cycling Stability Data for Drug Product PPQ Lot EL8723

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -20 ± 5°C (for 4 weeks)							
0[b]	WOS	Meets	(b) (4)				
2W	WOS	Meets					
4W	WOS	Meets					
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets	(b) (4)				
8W	WOS	Meets					
10W	S	S	S	S	S	S	S
12W	S	S	S	S	S	S	S
14W	S	S	S	S	S	S	S
16W	S	S	S	S	S	S	S

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -20 ± 5°C (for 4 weeks)						
0[b]	(b) (4)					
2W						
4W						
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W	(b) (4)					
8W						
10W	S	S	S	S	S	S
12W	S	S	S	S	S	S
14W	S	S	S	S	S	S
16W	S	S	S	S	S	S

Table 3.2.P.8.3-19. Thermal Cycling Stability Data for Drug Product PPQ Lot EL8723

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content

a. Acceptance criteria in place at time of testing.
b. Initial data (t0) are not from release testing. Analysis for t0 were repeated for this study.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-20. Thermal Cycling Stability Data for Drug Product PPQ Lot EL3249

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -90 to -60 °C (for 1 week)							
0	WOS	Meets	(b) (4)	(b) (4)			
At 1W, inventory moved to -20 ± 5 °C (for 2 weeks)							
3W	WOS	Meets	(b) (4)	(b) (4)			
Samples pulled for 3W testing. Inventory moved to 2 to 8 °C (for 4 weeks)							
4W	WOS	Meets	(b) (4)	(b) (4)			
5W	WOS	Meets	(b) (4)				
6W	WOS	Meets	(b) (4)				
7W	WOS	Meets	(b) (4)				
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)							
8W	WOS	Meets	(b) (4)	(b) (4)			

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -90 to -60 °C (for 1 week)						
0	(b) (4)					
At 1W, inventory moved to -20 ± 5 °C (for 2 weeks)						
3W	(b) (4)					
Samples pulled for 3W testing. Inventory moved to 2 to 8 °C (for 4 weeks)						
4W	(b) (4)					
5W						
6W						
7W						
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)						
8W	(b) (4)					

Table 3.2.P.8.3-20. Thermal Cycling Stability Data for Drug Product PPQ Lot EL3249

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content

a. Acceptance criteria in place at time of testing.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-21. Thermal Cycling Stability Data for Drug Product PPQ Lot EK4242

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -90 to -60 °C (for 1 week)							
0	WOS	Meets	(b) (4)	(b) (4)			
At 1W, inventory moved to 2 to 8 °C for remainder of study (4 weeks)							
2W	WOS	Meets	(b) (4)	(b) (4)			
3W	WOS	Meets	(b) (4)				
4W	WOS	Meets	(b) (4)				
5W	WOS	Meets	(b) (4)				

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -90 to -60 °C (for 1 week)						
0	(b) (4)					
At 1W, inventory moved to 2 to 8 °C for remainder of study (4 weeks)						
2W	(b) (4)					
3W						
4W						
5W						

a. Acceptance criteria in place at time of testing.
b. Initial data (t0) are not from release testing. Analysis for t0 were repeated for this study.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-22. Thermal Cycling Stability Data for Drug Product PPQ Lot EL7834

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Timepoint / Acceptance Criteria[a]	**White to off-white suspension**	**May contain white to off-white opaque, amorphous particles**	**7.4 ± 0.5**	(b) (4)			
Placed @ -90 to -60 °C (for 1 week)							
0	WOS	Meets	(b) (4)	(b) (4)			
At 1W, inventory moved to -20 ± 5 °C (for 4 weeks)							
3W	WOS	Meets	(b) (4)	(b) (4)			
5W	WOS	Meets	(b) (4)				
Samples pulled for 5W testing. Inventory moved to 2 to 8 °C (for 4 weeks)							
6W	WOS	Meets	(b) (4)	(b) (4)			
7W	WOS	Meets	(b) (4)				
8W	WOS	Meets	(b) (4)				
9W	WOS	Meets	(b) (4)				
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)							
10W	WOS	Meets	(b) (4)	(b) (4)			

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity
Timepoint / Acceptance Criteria[a]	(b) (4)					
Placed @ -90 to -60 °C (for 1 week)						
0	(b) (4)					
At 1W, inventory moved to -20 ± 5 °C (for 4 weeks)						
3W	(b) (4)					
5W						
Samples pulled for 5W testing. Inventory moved to 2 to 8 °C (for 4 weeks)						
6W	(b) (4)					
7W						
8W						
9W						
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)						
10W	(b) (4)					

Table 3.2.P.8.3-22. Thermal Cycling Stability Data for Drug Product PPQ Lot EL7834

Analytical Procedure/Quality Attribute	Appearance		pH	Dynamic Light Scattering (DLS)		Fluorescence Assay	
	Appearance (Visual)	Visible Particulates		LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content

a. Acceptance criteria in place at time of testing.
b. Initial data (t0) are not from release testing. Analysis for t0 were repeated for this study.
W = Week, S = To be Scheduled, (b) (4), LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension