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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/ $60 \pm 5\%$ RH and 30 ± 2 °C/ $65 \pm 5\%$ 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) and Pfizer, Puurs.

Additionally, data from supportive stability studies for one clinical BNT162b2 drug product lot and one clinical supportive BNT162b1 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.8.3-27.

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 (February 2021 for Thermal Cycling Study 1 and April 2021 for Thermal Cycling Studies 2 & 3)	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
			Thermal Cycling 1: 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.		16 weeks (On-going)	Table 3.2.P.8.3-19
			Thermal Cycling 2: Ultra frozen vials are placed at -20 ± 5 °C for 4 weeks (1 month) and then moved to -90 to -60 °C for the shelf life of the drug product.		1 month	Table 3.2.P.8.3-24
			Thermal Cycling 3: Ultra frozen vials are placed at 5 ± 3 °C for 4 weeks (1 month) and then moved to -90 to -60 °C for the shelf life of the drug product.		1 month	Table 3.2.P.8.3-25
			Ultrafrozen vials were cycled between 25 ± 2 °C/60 ± 5%RH (for 2 to 7 hours) and -90 to -60 °C (for 24 ± 2 hours) for a total of 10 cycles		10 freeze thaw cycles	Table 3.2.P.8.3-26
EL3248 (Pfizer, Kalamazoo)	Stability, Clinical, Emergency Supply ^a , Process performance qualification	December 2020	Thermal Stress		25 ± 2 °C/60 ± 5% RH	Table 3.2.P.8.3-11
			Thermal Stress		30 ± 2 °C/65 ± 5% RH	Table 3.2.P.8.3-12
ET0384 (Polymun/Pfizer, Puurs)	Stability, Emergency Supply ^a , Process performance qualification	February 2021	Thermal Cycling: Ultra frozen vials are placed at -90 to -60 °C for 5 months and then a subset of vials moved to 2 to 8°C for 1 month. Samples pulled at 6M for testing at both -90 to -60°C and 2 to 8°C. This is repeated at 11/12M, 17/18M and 23/24M		Release	Table 3.2.P.8.3-27
EL3249 (Pfizer, Kalamazoo)	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.8.3-23
EL9266 (Pfizer, Kalamazoo)	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.		16 weeks	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
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.		12 weeks (On-going)	Table 3.2.P.8.3-18
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.8.3-20
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.8.3-21
EH9899 (Pfizer, Kalamazoo)	Stability, Emergency Supply ^a	November 2020	Thermal Stress	25 ± 2 °C/ 60 ± 5 % RH	1 month (Complete)	Table 3.2.P.8.3-13
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.8.3-4
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.8.3-5
			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
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.8.3-6
			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.8.3-17
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.8.3-7
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.8.3-8

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
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.8.3-9
			Thermal Stress	30 ± 2 °C/65 ± 5% RH	1 month (Complete)	Table 3.2.P.8.3-10
BCV40420-A (Polymun Scientific)	Stability, Clinical	May 2020	Thermal Stress	25 ± 2 °C	4 months (complete)	Table 3.2.P.8.3-14
Supportive Lots (BNT162b1)						
BCV10320-A (Polymun Scientific)	Supportive Stability, Clinical	April 2020	Thermal Stress	25 ± 2 °C	3 months (complete)	Table 3.2.P.8.3-15

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 (Pfizer, Puurs)

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					
0	WOS	Meets (EFVP)					
1W	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
1M	WOS	Meets (EFVP)					

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						
0						
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing.

W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; EFVP = Essentially free from visible particulates; 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/ $65 \pm 5\%$ RH (Pfizer, Puurs)

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					
0	WOS	Meets (EFVP)					
1W	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
1M	WOS	Meets (EFVP)					

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						
0						
1W						
2W						
1M						

a. Acceptance criteria in place at time of testing. Updated at the 1 month time point.

W = Week, M = Month, S = To be Scheduled, NS = Not Scheduled at Time Point; EFVP = Essentially free from visible particulates; 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 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					
0	White to off-white suspension	EFVP					
1W	White to off-white suspension	EFVP					
2W	White to off-white suspension	EFVP					
1M	White to off-white suspension	Meets (EFVP)					

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						
0						
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; EFVP = Essentially free from visible particulates; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-5. Stability Data for Drug Product Emergency Supply Batch EK1768 Stored at 25 ± 2 °C/ $60 \pm 5\%$ 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					
0	White to off-white suspension	EFVP					
1W	White to off-white suspension	Meets (EFVP)					
2W	White to off-white suspension	Meets (EFVP)					
1M	White to off-white suspension	Meets (EFVP)					

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						
0						
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; EFVP = Essentially free from visible particulates; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

Table 3.2.P.8.3-6. Stability Data for Drug Product Emergency Supply Batch EJ1686 Stored at $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{ RH}$

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					
0 ^b	White to off-white suspension	EFVP					
1W	White to off-white suspension	Meets (EFVP)					
2W	White to off-white suspension	Meets (EFVP)					
1M	White to off-white suspension	Meets (EFVP)					

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						
0 ^b						
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; EFVP = Essentially free from visible particulates; 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 EJ1685 Stored at $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{RH}$

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					
0	White to off-white suspension	EFVP					
1W	White to off-white suspension	EFVP					
2W	White to off-white suspension	Meets (EFVP)					
1M	White to off-white suspension	Meets (EFVP)					

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						
0						
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; EFVP = Essentially free from visible particulates; 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 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					
0	White to off-white suspension	EFVP					
1W	White to off-white suspension	EFVP					
2W	White to off-white suspension	EFVP					
1M	White to off-white suspension	EFVP					

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						
0						
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; EFVP = Essentially free from visible particulates; 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 Lot EE8493 Stored at $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{ RH}$

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	EFVP					
0	White to off-white suspension	EFVP					
2W	White to off-white suspension	EFVP					
1M	White to off-white suspension	EFVP					

Time	HPLC-CAD				Cell-based FACS	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	$\geq 50\%$ intact RNA
0						
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, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, MCR = Meets Compendial Requirements

Table 3.2.P.8.3-10. Stability Data for Drug Product Emergency Supply Lot EE8493 Stored at 30 ± 2 °C/ $65 \pm 5\%$ 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	EFVP					
0	White to off-white suspension	EFVP					
2W	White to off-white suspension	EFVP					
1M	White to off-white suspension	EFVP					

Time	HPLC-CAD				Cell-based FACS	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	≥ 50% intact RNA
0						No Result ^b
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, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, MCR = Meets Compendial Requirements

Table 3.2.P.8.3-11. Stability Data for Drug Product PPQ Lot EL3248 Stored at 25 ± 2 °C/60 ± 5% RH (Pfizer, Kalamazoo)

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					
0	WOS	Meets (EFVP)					
1W	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
3W	WOS	Meets (EFVP)					
1M	WOS	Meets (EFVP)					

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						
0						
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; EFVP = Essentially free from visible particulates; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-12. Stability Data for Drug Product PPQ Lot EL3248 Stored at 30 ± 2 °C/ 65 ± 5 % RH (Pfizer, Kalamazoo)

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					
0	WOS	Meets (EFVP)					
1W	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
3W	WOS	Meets (EFVP)					
1M	WOS	Meets (EFVP)					

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						
0						
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; EFVP = Essentially free from visible particulates; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-13. Stability Data for Drug Product Emergency Supply Batch EH9899 Stored at 25 ± 2 °C/ $60 \pm 5\%$ 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					
0 ^b	White to off-white suspension	EFVP					
1W	White to off-white suspension	EFVP					
2W	White to off-white suspension	EFVP					
1M	White to off-white suspension	EFVP					

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						No Result ^c
0 ^b						
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; EFVP = Essentially free from visible particulates; LNP = Lipid Nanoparticle; HPLC-CAD = high performance liquid chromatography-charged aerosol detector

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					
0	Pass					
0.5	Pass					
1	Pass					
2	Pass					
3	Pass					
4	Pass					

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)	≥ 60%
0					
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. Stability Data for Polymun Scientific Drug Product BNT162b1 Lot BCV10320-A Stored at 25 ± 2 °C

Time (Month)	Appearance	pH	LNP Size	LNP Polydispersity	RNA Encapsulation	RNA Content
Acceptance Criteria ^a	White to off-white suspension/Free from observable particles					
0	Pass					
0.5	Pass					
1	Pass					
2	Pass					
3	Pass					

Time (Month)	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)	≥ 60%
0					
0.5					
1					
2					
3					

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

Table 3.2.P.8.3-16. 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					
Placed @ -90 to -60°C (for 2 weeks)							
0	WOS	EFVP					
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)							
2W	WOS	Meets (EFVP)					
4W	WOS	Meets (EFVP)					
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets (EFVP)					
8W	WOS	Meets (EFVP)					
10W	WOS	Meets (EFVP)					
12W	WOS	Meets (EFVP)					
14W	WOS	Meets (EFVP)					

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						
Placed @ -90 to -60°C (for 2 weeks)						
0						
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)						
2W						
4W						
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W						
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, EFVP = Essentially free from visible particulates, 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 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					
Placed @ -90 to -60°C (for 2 weeks)							
0 ^b	WOS	EFVP					
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)							
2W	WOS	Meets (EFVP)					
4W	WOS	Meets (EFVP)					
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets (EFVP)					
8W	WOS	Meets (EFVP)					
10W	WOS	Meets (EFVP)					
12W	WOS	Meets (EFVP)					
14W	WOS	Meets (EFVP)					

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						
Placed @ -90 to -60°C (for 2 weeks)						
0 ^b						
Samples pulled for 2W testing. Inventory moved to -20 ± 5°C (for 4 weeks)						
2W						
4W						
Samples pulled for 6W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W						
8W						
10W						
12W						
14W						

Table 3.2.P.8.3-17. 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, EFVP = Essentially free from visible particulates, 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 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					
Placed @ -20 ± 5°C (for 4 weeks)							
0	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
4W	WOS	Meets (EFVP)					
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets (EFVP)					
8W	WOS	Meets (EFVP)					
10W	WOS	Meets (EFVP)					
12W	WOS	Meets (EFVP)					
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						
Placed @ -20 ± 5°C (for 4 weeks)						
0						
2W						
4W						
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W						
8W						
10W						
12W						
14W	S	S	S	S	S	S
16W	S	S	S	S	S	S

a. Acceptance criteria in place at time of testing.

W = Week, S = To be Scheduled, EFVP = Essentially free from visible particulates, 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					
Placed @ -20 ± 5°C (for 4 weeks)							
0 ^b	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
4W	WOS	Meets (EFVP)					
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets (EFVP)					
8W	WOS	Meets (EFVP)					
10W	WOS	Meets (EFVP)					
12W	WOS	Meets (EFVP)					
14W	WOS	Meets (EFVP)		Pending	Pending		
16W	WOS	Meets (EFVP)		Pending	Pending		

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						
Placed @ -20 ± 5°C (for 4 weeks)						
0 ^b						
2W						
4W						
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W						
8W						
10W						
12W						
14W						
16W	Pending	Pending	Pending	Pending		

a. Acceptance criteria in place at time of testing.

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

b. Initial data (t0) are not from release testing. Analysis for t0 were repeated for this study.

c. Original result investigated and invalidated. Reference PR 5889739

W = Week, S = To be Scheduled, EFVP = Essentially free from visible particulates, 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 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					
Placed @ -90 to -60 °C (for 1 week)							
0	WOS	Meets (EFVP)					
At 1W, inventory moved to 2 to 8 °C for remainder of study (4 weeks)							
2W	WOS	Meets (EFVP)					
3W	WOS	Meets (EFVP)					
4W	WOS	Meets (EFVP)					
5W	WOS	Meets (EFVP)					

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						
Placed @ -90 to -60 °C (for 1 week)						
0						
At 1W, inventory moved to 2 to 8 °C for remainder of study (4 weeks)						
2W						
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, EFVP = Essentially free from visible particulates, 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 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					
Placed @ -90 to -60 °C (for 1 week)							
0	WOS	Meets (EFVP)					
At 1W, inventory moved to -20 ± 5 °C (for 4 weeks)							
3W	WOS	Meets (EFVP)					
5W	WOS	Meets (EFVP)					
Samples pulled for 5W testing. Inventory moved to 2 to 8 °C (for 4 weeks)							
6W	WOS	Meets (EFVP)					
7W	WOS	Meets (EFVP)					
8W	WOS	Meets (EFVP)					
9W	WOS	Meets (EFVP)					
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)							
10W	WOS	Meets (EFVP)					

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						
Placed @ -90 to -60 °C (for 1 week)						
0						
At 1W, inventory moved to -20 ± 5 °C (for 4 weeks)						
3W						
5W						
Samples pulled for 5W testing. Inventory moved to 2 to 8 °C (for 4 weeks)						
6W						
7W						
8W						
9W						
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)						
10W						

Table 3.2.P.8.3-21. 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, EFVP = Essentially free from visible particulates, 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 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					
Placed @ -20 ± 5°C (for 4 weeks)							
0 ^b	WOS	Meets (EFVP)					
2W	WOS	Meets (EFVP)					
4W	WOS	Meets (EFVP)					
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study							
6W	WOS	Meets (EFVP)					
8W	WOS	Meets (EFVP)					
10W	WOS	Meets (EFVP)					
12W	WOS	Meets (EFVP)					
14W	WOS	Meets (EFVP)		Pending	Pending		
16W	WOS	Meets (EFVP)		Pending	Pending		

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						
Placed @ -20 ± 5°C (for 4 weeks)						
0 ^b						
2W						
4W						
Samples pulled for 4W testing. Inventory moved to 2 to 8 °C for remainder of study						
6W						
8W						
10W						
12W						
14W						
16W	Pending	Pending	Pending	Pending		

Table 3.2.P.8.3-22. 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.

c. Original result investigated and invalidated. Reference PR 5889739

W = Week, S = To be Scheduled, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-23. 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					
Placed @ -90 to -60 °C (for 1 week)							
0	WOS	Meets (EFVP)					
At 1W, inventory moved to -20 ± 5 °C (for 2 weeks)							
3W	WOS	Meets (EFVP)					
Samples pulled for 3W testing. Inventory moved to 2 to 8 °C (for 4 weeks)							
4W	WOS	Meets (EFVP)					
5W	WOS	Meets (EFVP)					
6W	WOS	Meets (EFVP)					
7W	WOS	Meets (EFVP)					
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)							
8W	WOS	Meets (EFVP)					

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						
Placed @ -90 to -60 °C (for 1 week)						
0						
At 1W, inventory moved to -20 ± 5 °C (for 2 weeks)						
3W						
Samples pulled for 3W testing. Inventory moved to 2 to 8 °C (for 4 weeks)						
4W						
5W						
6W						
7W						
Samples pulled for 7W testing. Inventory moved to 25 ± 2 °C/60 ± 5% RH (for 1 week)						
8W						

Table 3.2.P.8.3-23. 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, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-24. Thermal Cycling Stability Data for Drug Product PPQ Lot EL8723 (-20 ± 5 °C)

Analytical Procedure/Quality Attribute	Appearance		pH	Subvisible Particles ^b	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						
Ultrafrozen vials placed -20 ± 5 °C (for 1 month)								
0	WOS	Meets (EFVP)						
2W	WOS	Meets (EFVP)						
4W	WOS	Meets (EFVP)		Pending	Pending	Pending		
Inventory moved to -90 to -60 °C (for remainder of study)								
6M	S	S	S	S	S	S	S	S
12M	S	S	S	S	S	S	S	S
18M	S	S	S	S	S	S	S	S
24M	S	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						
Ultrafrozen vials placed -20 ± 5 °C (for 1 month)						
0						
2W						
4W	Pending	Pending	Pending	Pending	Pending	
Inventory moved to -90 to -60 °C (for remainder of study)						
6M	S	S	S	S	S	S
12M	S	S	S	S	S	S
18M	S	S	S	S	S	S
24M	S	S	S	S	S	S

Table 3.2.P.8.3-24. Thermal Cycling Stability Data for Drug Product PPQ Lot EL8723 (-20 ± 5 °C)

Analytical Procedure/Quality Attribute	Appearance		pH	Subvisible Particles ^b	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. Subvisible particles are reported per container

W = Week, S = To be Scheduled, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-25. Thermal Cycling Stability Data for Drug Product PPQ Lot EL8723 (2 to 8 °C)

Analytical Procedure/Quality Attribute	Appearance		pH	Subvisible Particles ^b	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						
Ultrafrozen vials placed 2 to 8 °C (for 1 month)								
0	WOS	Meets (EFVP)						
2W	WOS	Meets (EFVP)						
4W	WOS	Meets (EFVP)		Pending	Pending	Pending		
Inventory moved to -90 to -60 °C (for remainder of study)								
6M	S	S	S	S	S	S	S	S
12M	S	S	S	S	S	S	S	S
18M	S	S	S	S	S	S	S	S
24M	S	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						
Ultrafrozen vials placed 2 to 8 °C (for 1 month)						
0						
2W						
4W	Pending	Pending	Pending	Pending	Pending	
Inventory moved to -90 to -60 °C (for remainder of study)						
6M	S	S	S	S	S	S
12M	S	S	S	S	S	S
18M	S	S	S	S	S	S
24M	S	S	S	S	S	S

a. Acceptance criteria in place at time of testing.

b. Subvisible particles are reported per container

W = Week, S = To be Scheduled, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-26. Freeze Thaw Cycling Stability Data for Drug Product PPQ Lot EL8723

Analytical Procedure/Quality Attribute	Appearance		pH	Subvisible Particles ^b	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						
Ultrafrozen vials were cycled between 25 ± 2 °C/60 ± 5%RH (for 2 to 7 hours) and -90 to -60 °C (for 24 ± 2 hours) for a total of 10 cycles								
0	WOS	Meets (EFVP)						
Cycle 1	WOS	Meets (EFVP)						
Cycle 4	WOS	Meets (EFVP)						
Cycle 7	WOS	Meets (EFVP)						
Cycle 10	WOS	Meets (EFVP)						

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						
Ultrafrozen vials were cycled between 25 ± 2 °C/60 ± 5%RH (for 2 to 7 hours) and -90 to -60 °C (for 24 ± 2 hours) for a total of 10 cycles						
0						
Cycle 1						
Cycle 4						
Cycle 7						
Cycle 10						

a. Acceptance criteria in place at time of testing.

b. Subvisible particles are reported per container.

W = Week, S = To be Scheduled, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension

Table 3.2.P.8.3-27. Thermal Cycling Stability Data for Drug Product PPQ Lot ET0384

Analytical Procedure/Quality Attribute	Appearance		pH	Subvisible Particles ^b	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						
Ultrafrozen vials placed -90 to -60 °C. @ 5 month timepoint, vials for 6 month testing moved to 2 to 8 °C for one month								
0	WOS	Meets (EFVP)						
6M -90 to -60 °C	S	S	S	S	S	S	S	S
6M 2 to 8 °C	S	S	S	S	S	S	S	S
@ 11 month timepoint, vials for 12 month testing moved to 2 to 8 °C for one month								
12M -90 to -60 °C	S	S	S	S	S	S	S	S
12M 2 to 8 °C	S	S	S	S	S	S	S	S
@ 17 month timepoint, vials for 18 month testing moved to 2 to 8 °C for one month								
18M -90 to -60 °C	S	S	S	S	S	S	S	S
18M 2 to 8 °C	S	S	S	S	S	S	S	S
@ 23 month timepoint, vials for 24 month testing moved to 2 to 8 °C for one month								
24M -90 to -60 °C	S	S	S	S	S	S	S	S
24M 2 to 8 °C	S	S	S	S	S	S	S	S

Analytical Procedure/Quality Attribute	HPLC-CAD				Cell-based Flow Cytometry	Capillary Gel Electrophoresis	Dye Incursion	Endotoxin	Sterility
	ALC-0315 Content	ALC-0159 Content	DSPC Content	Cholesterol Content	In Vitro Expression	RNA Integrity	Dye Ingress		
Timepoint / Acceptance Criteria ^a									
Ultrafrozen vials placed -90 to -60 °C. @ 5 month timepoint, vials for 6 month testing moved to 2 to 8 °C for one month									
0									
6M -90 to -60 °C	S	S	S	S	S	S	S	NS	NS
6M 2 to 8 °C	S	S	S	S	S	S	S	NS	NS
@ 11 month timepoint, vials for 12 month testing moved to 2 to 8 °C for one month									
12M -90 to -60 °C	S	S	S	S	S	S	S	S	S
12M 2 to 8 °C	S	S	S	S	S	S	S	S	S
@ 17 month timepoint, vials for 18 month testing moved to 2 to 8 °C for one month									

Table 3.2.P.8.3-27. Thermal Cycling Stability Data for Drug Product PPQ Lot ET0384

18M -90 to -60 °C	S	S	S	S	S	S	S	NS	NS
18M 2 to 8 °C	S	S	S	S	S	S	S	NS	NS
@ 23 month timepoint, vials for 24 month testing moved to 2 to 8 °C for one month									
24M -90 to -60 °C	S	S	S	S	S	S	S	S	S
24M 2 to 8 °C	S	S	S	S	S	S	S	S	S

a. Acceptance criteria in place at time of testing.

b. Subvisible particles are reported per container.

W = Week, M = Month, S = To be Scheduled, EFVP = Essentially free from visible particulates, LNP = Lipid Nanoparticle, HPLC-CAD = high performance liquid chromatography-charged aerosol detector, WOS = White to off-white suspension, NGD = No growth detected