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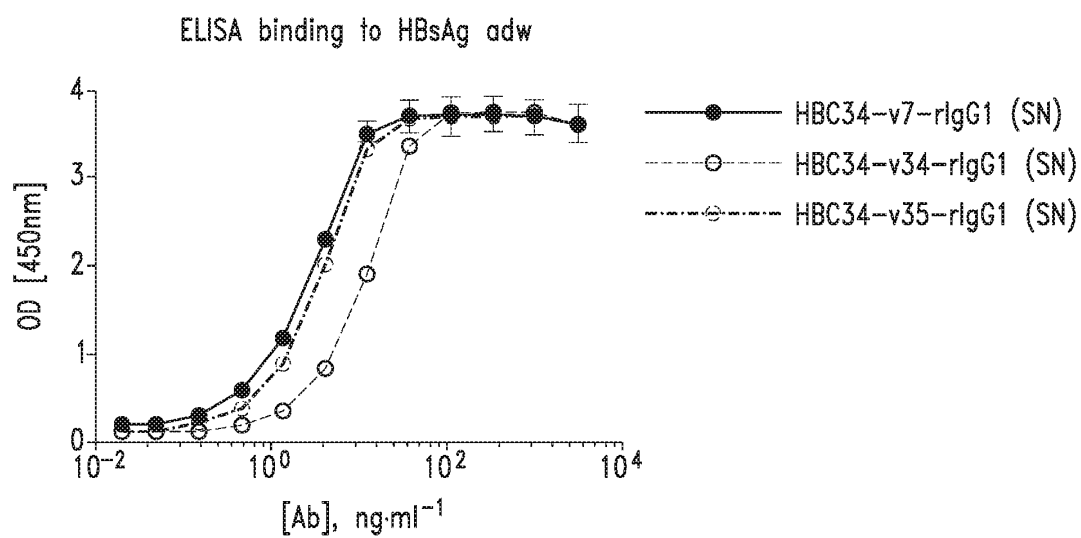


FIG. 1A

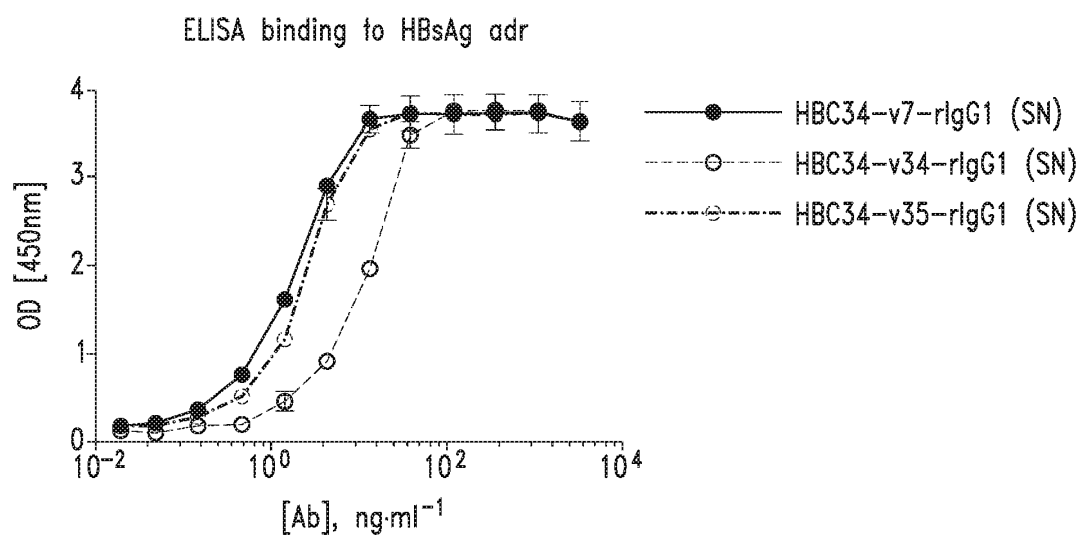


FIG. 1B

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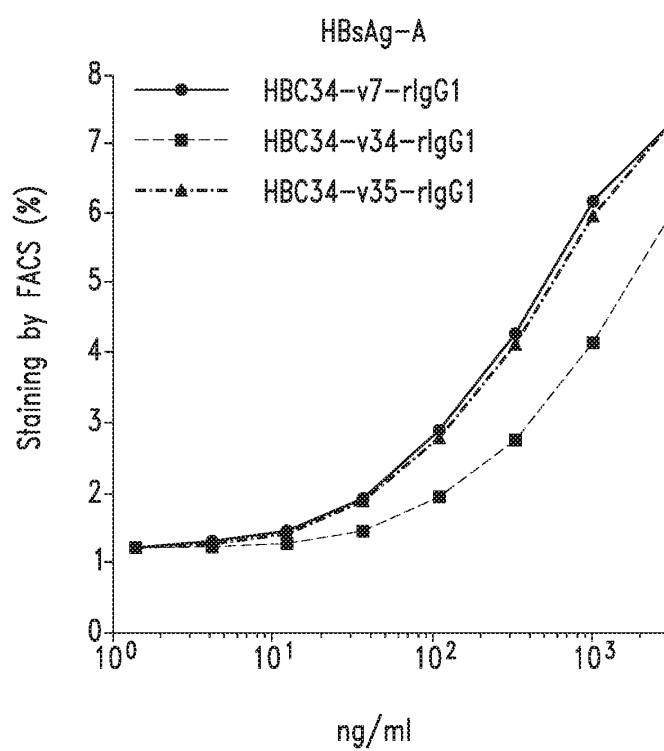
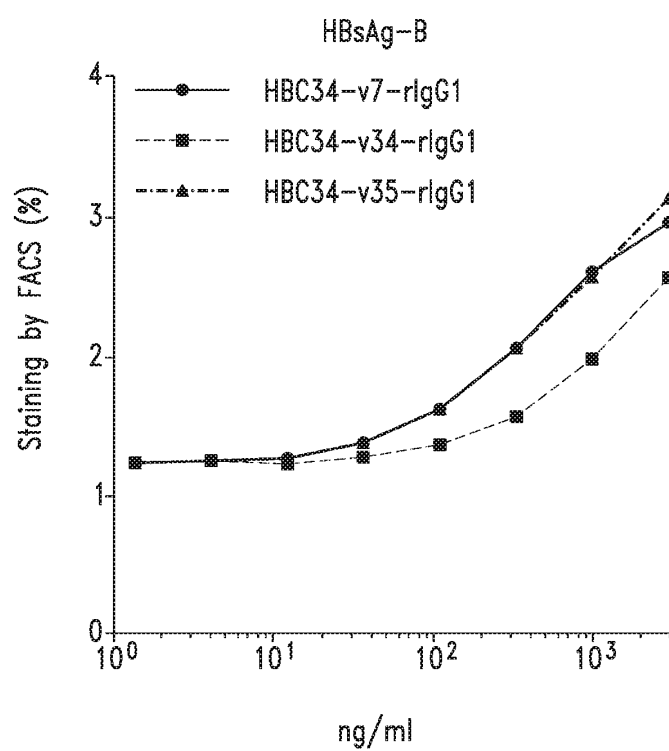


FIG. 2A

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*FIG. 2B*

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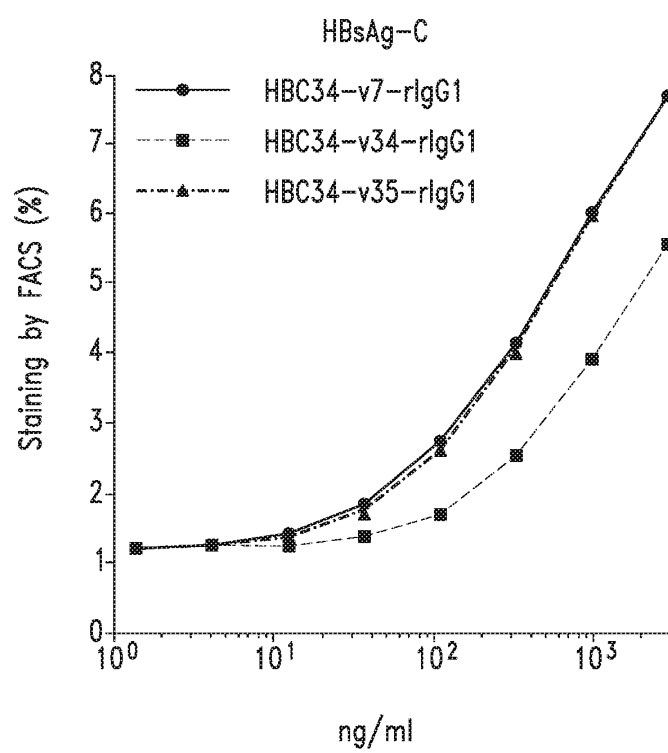
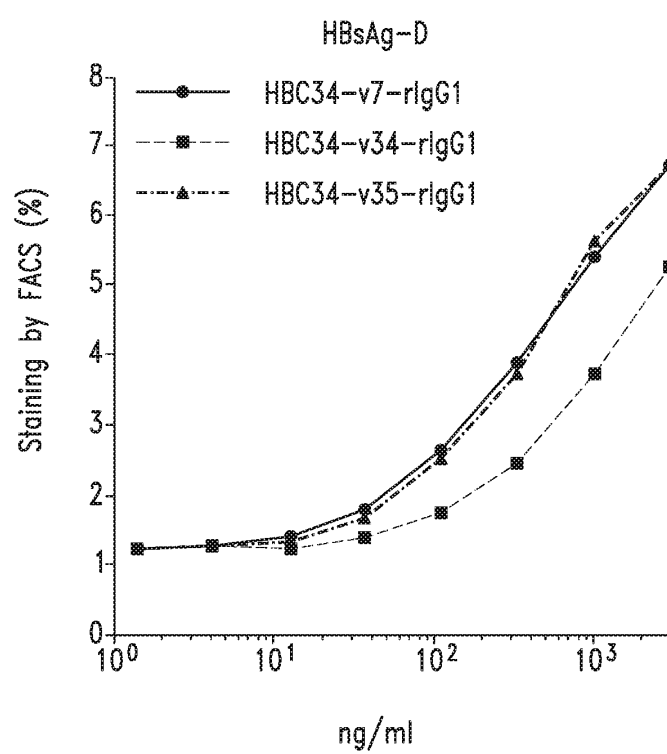
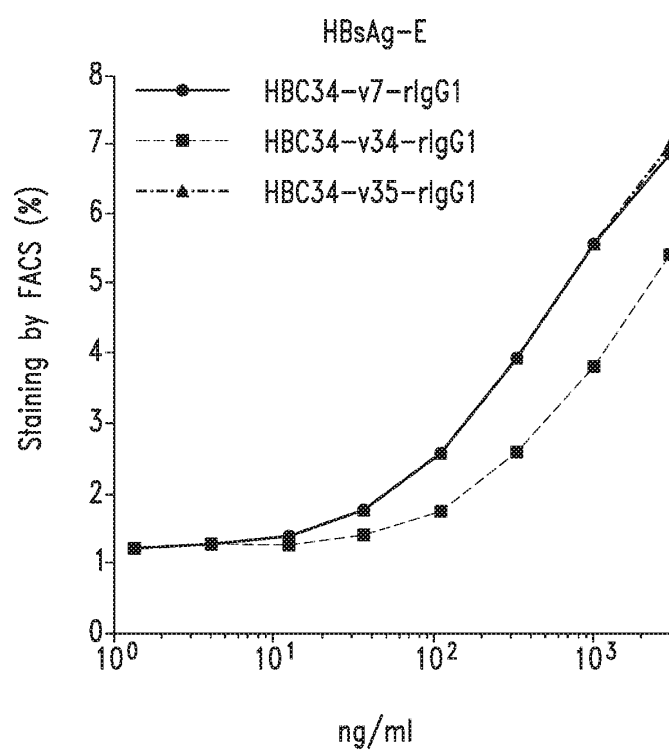


FIG. 2C

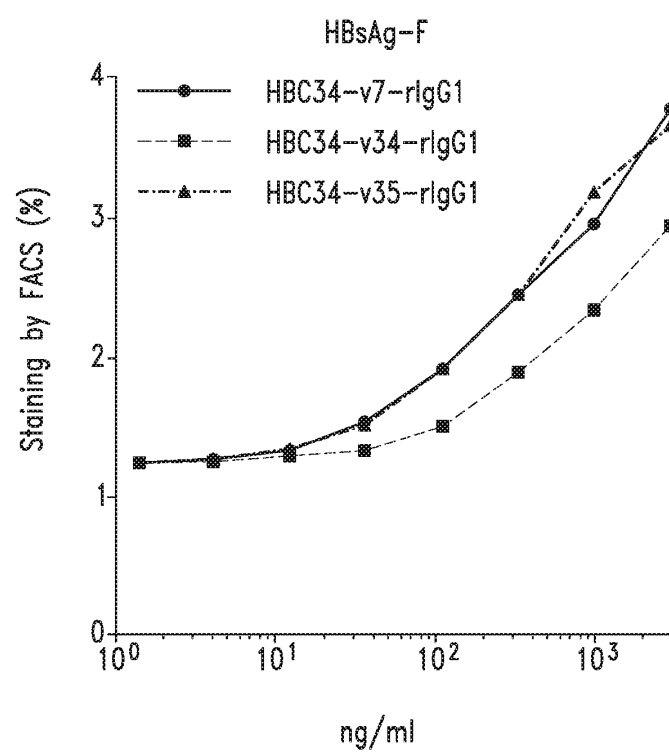
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*FIG. 2D*

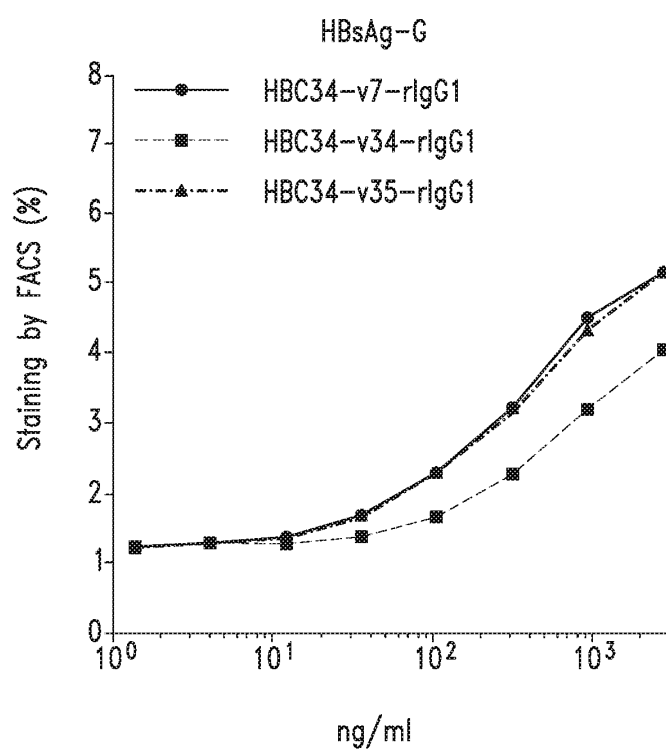
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*FIG. 2E*

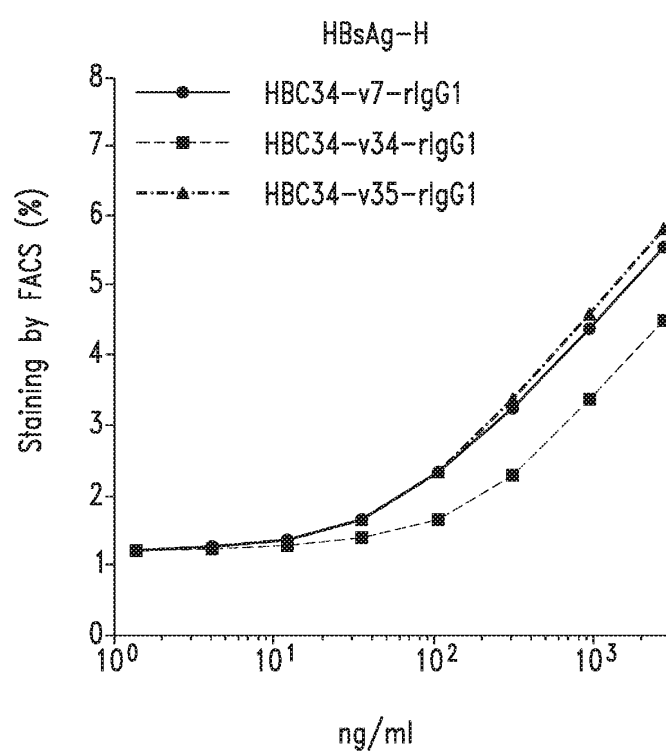
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*FIG. 2F*

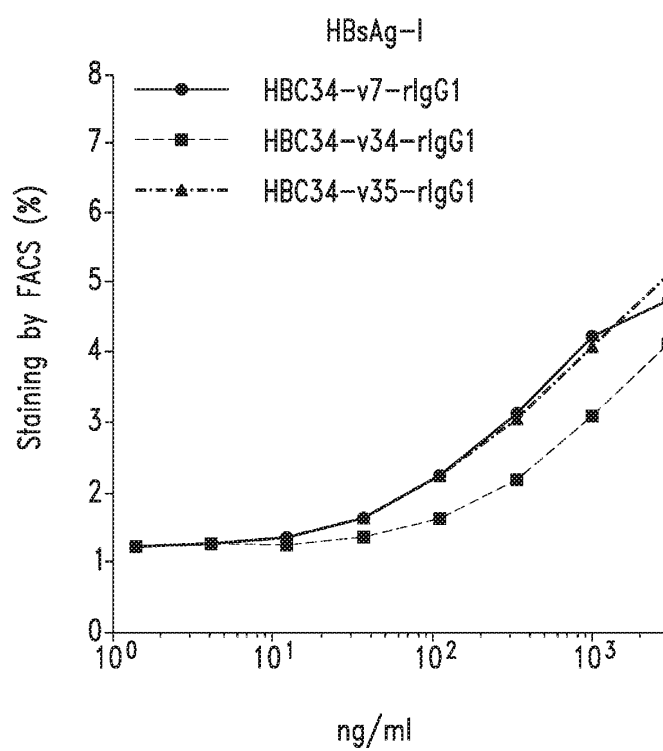
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*FIG. 2G*

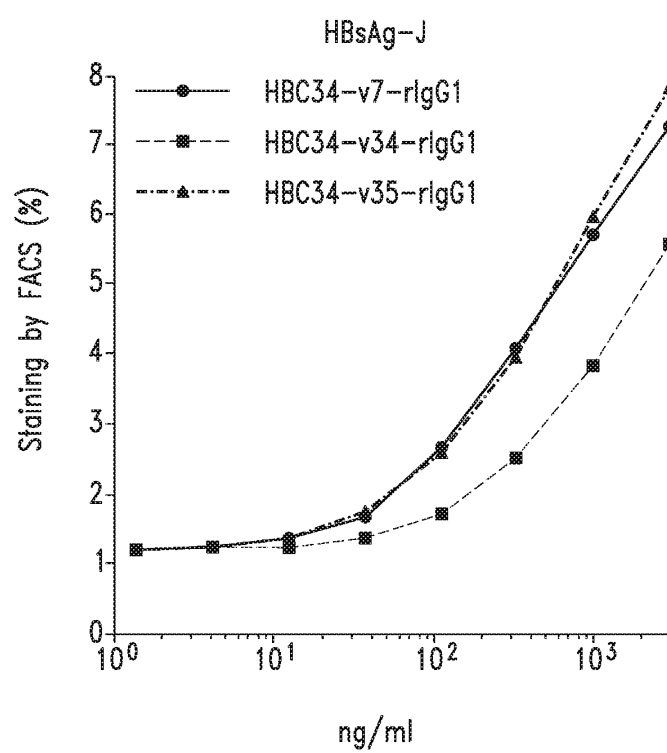
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*FIG. 2H*

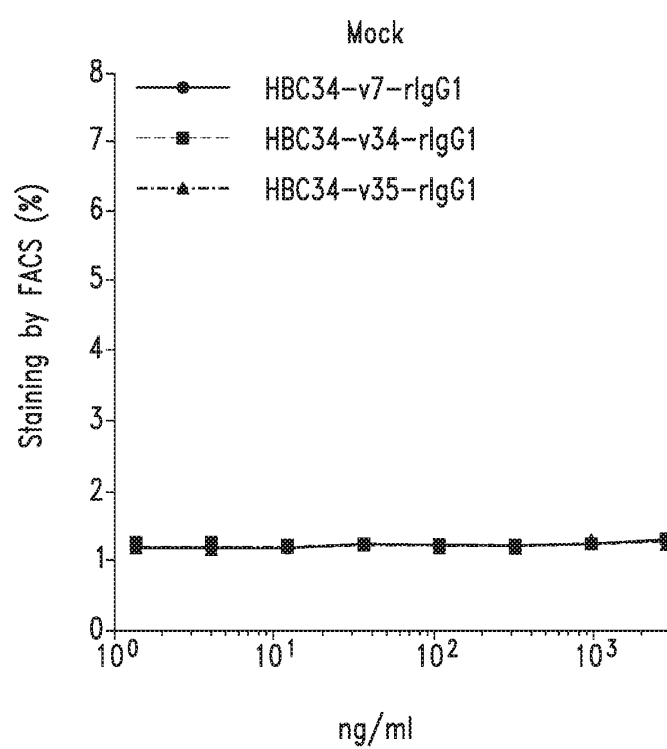
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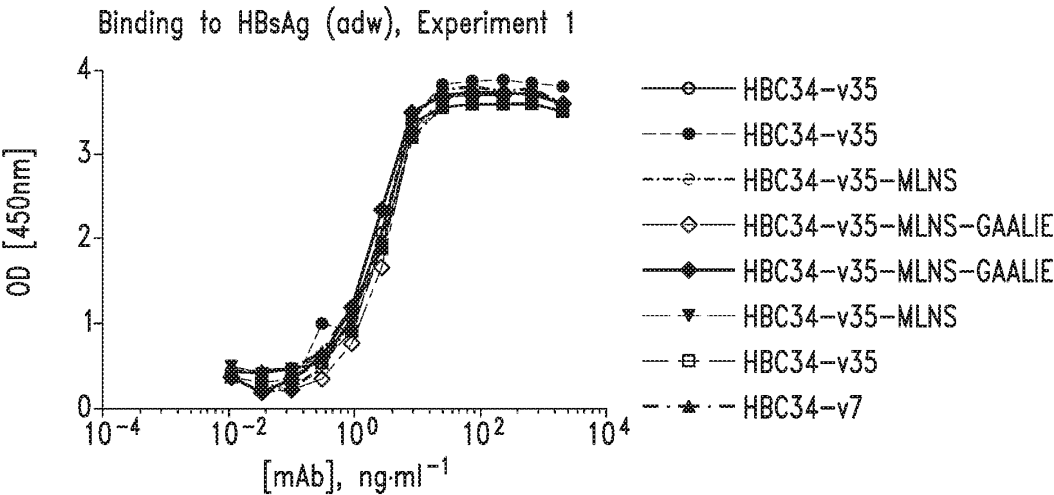
*FIG. 2I*

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*FIG. 2J*

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*FIG. 2K*



	EC50
HBC34-v35	2.43
HBC34-v35	2.799
HBC34-v35-MLNS	2.565
HBC34-v35-MLNS-GAALIE	3.186
HBC34-v35-MLNS-GAALIE	1.982
HBC34-v35-MLNS	2.309
HBC34-v35	2.662

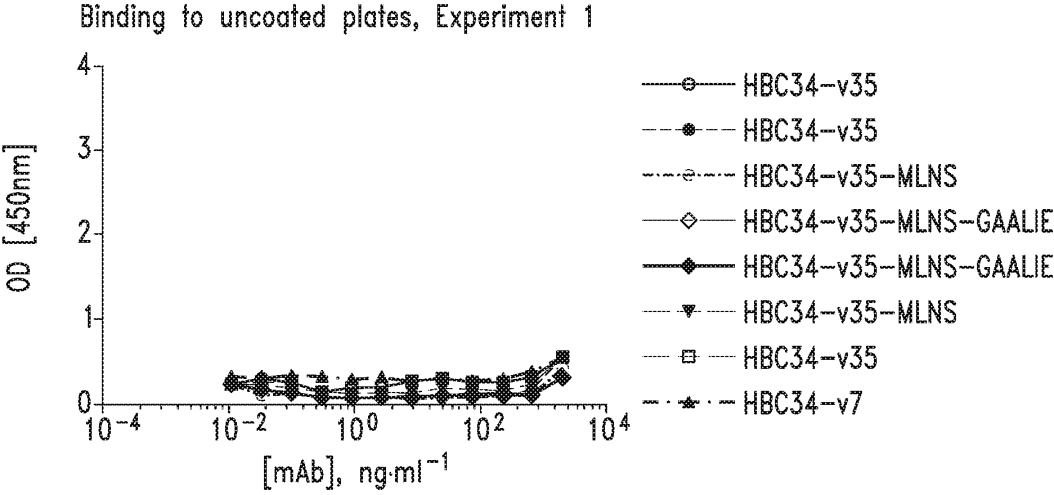
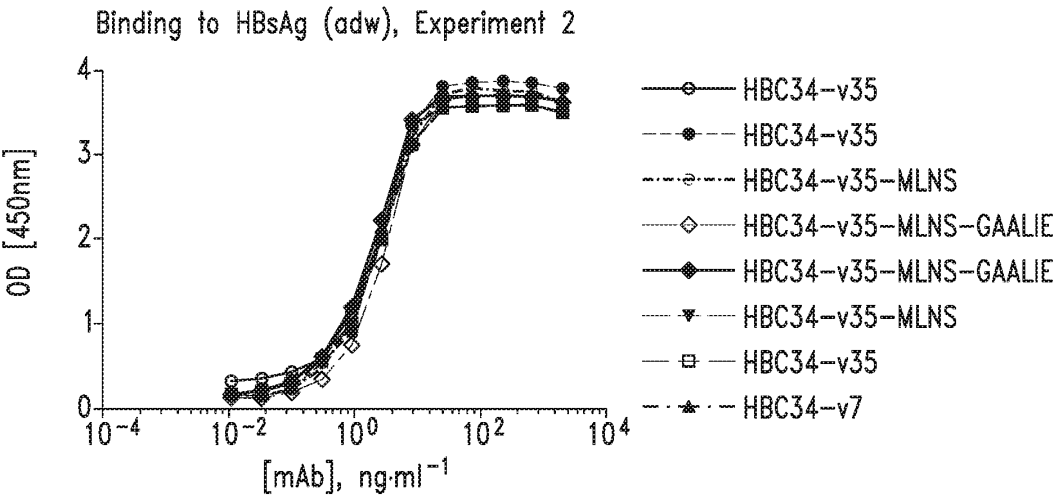


FIG. 3A



	EC50
HBC34-v35	2.278
HBC34-v35	2.651
HBC34-v35-MLNS	2.484
HBC34-v35-MLNS-GAALIE	3.018
HBC34-v35-MLNS-GAALIE	1.958
HBC34-v35-MLNS	2.174
HBC34-v35	2.358

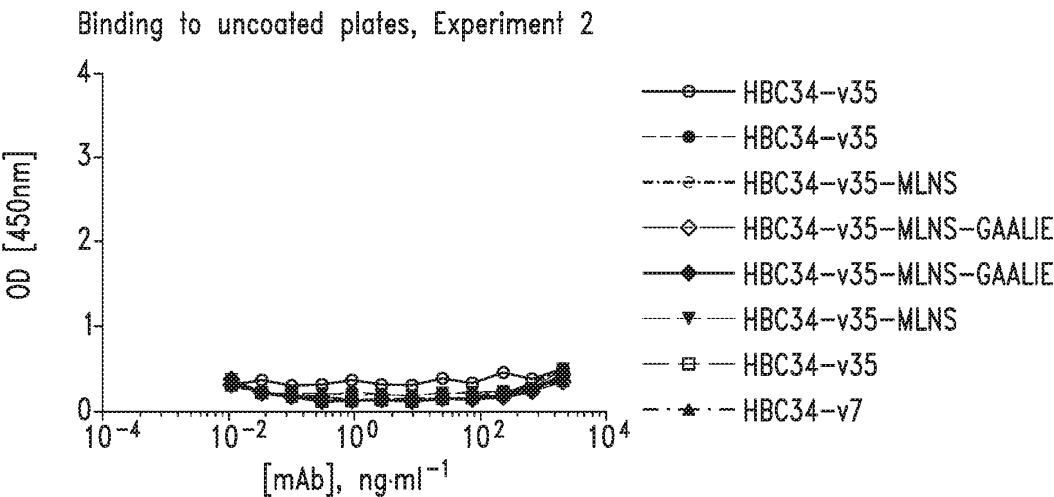


FIG. 3B

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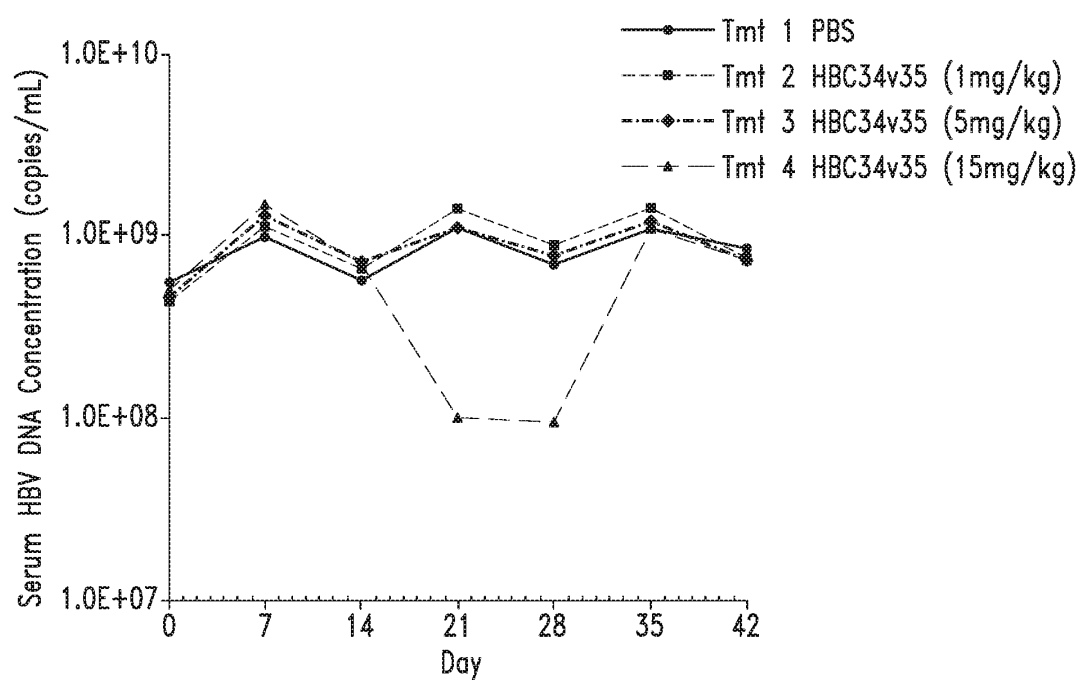


FIG. 4

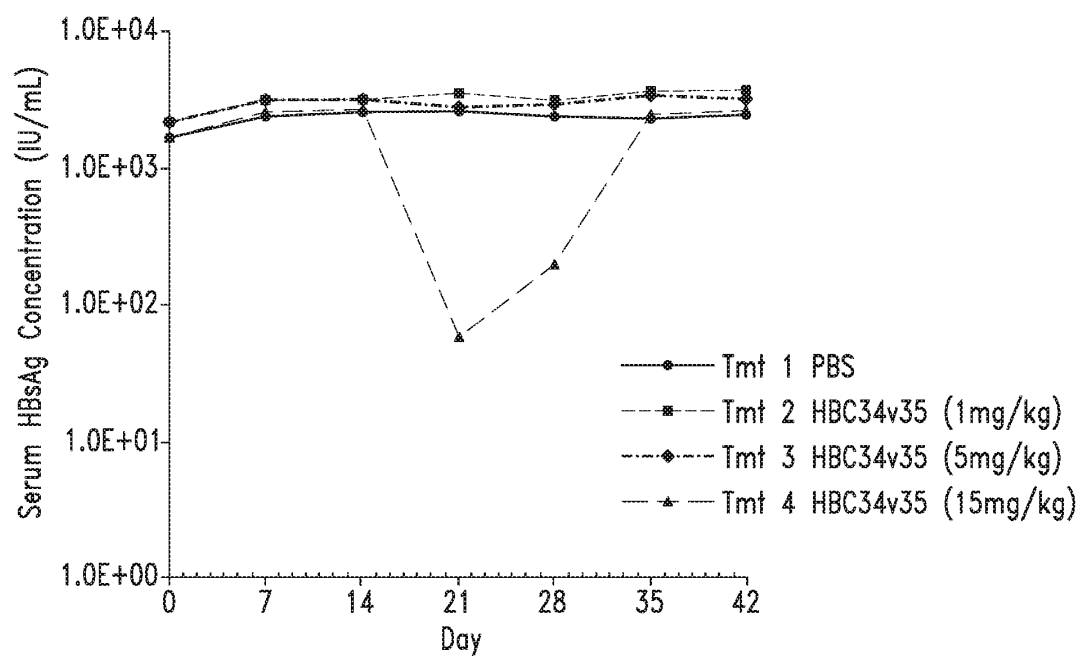


FIG. 5

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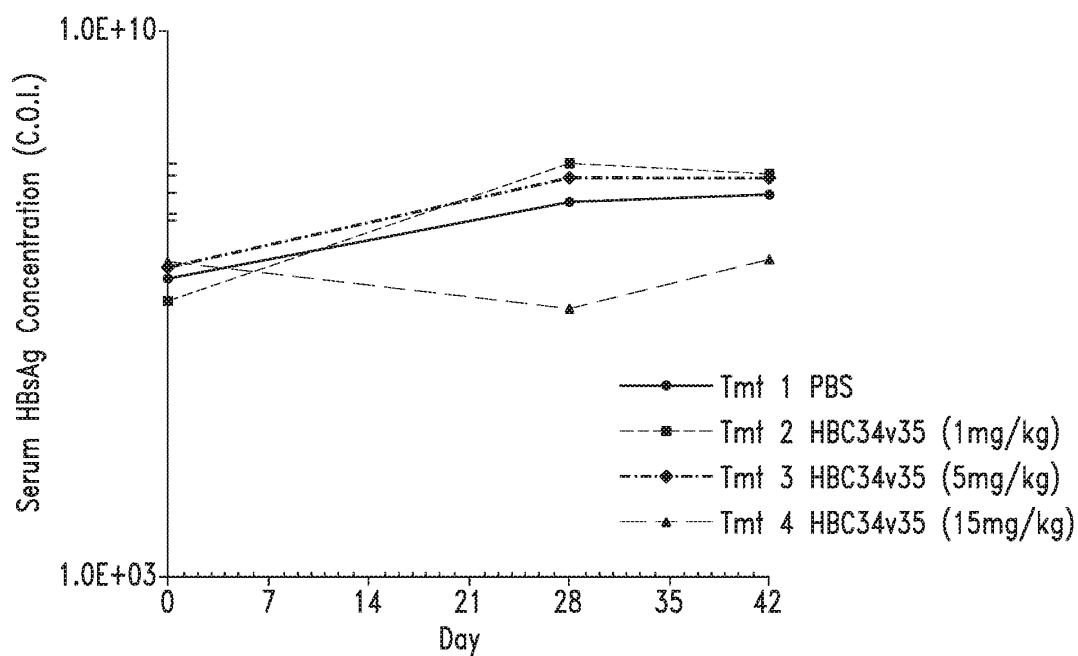


FIG. 6

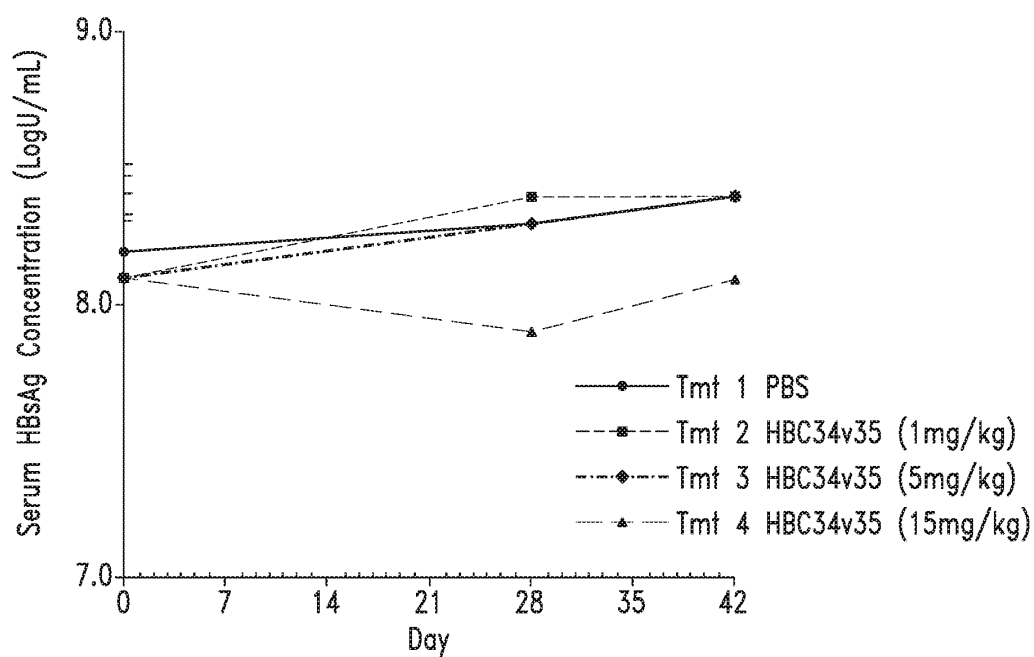


FIG. 7

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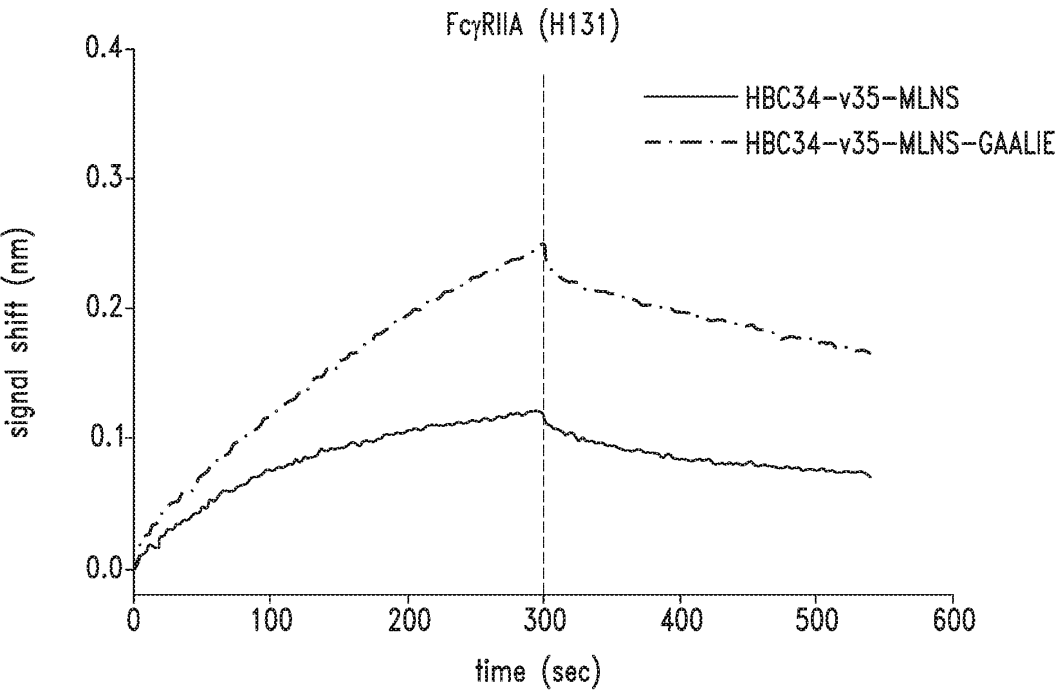


FIG. 8A

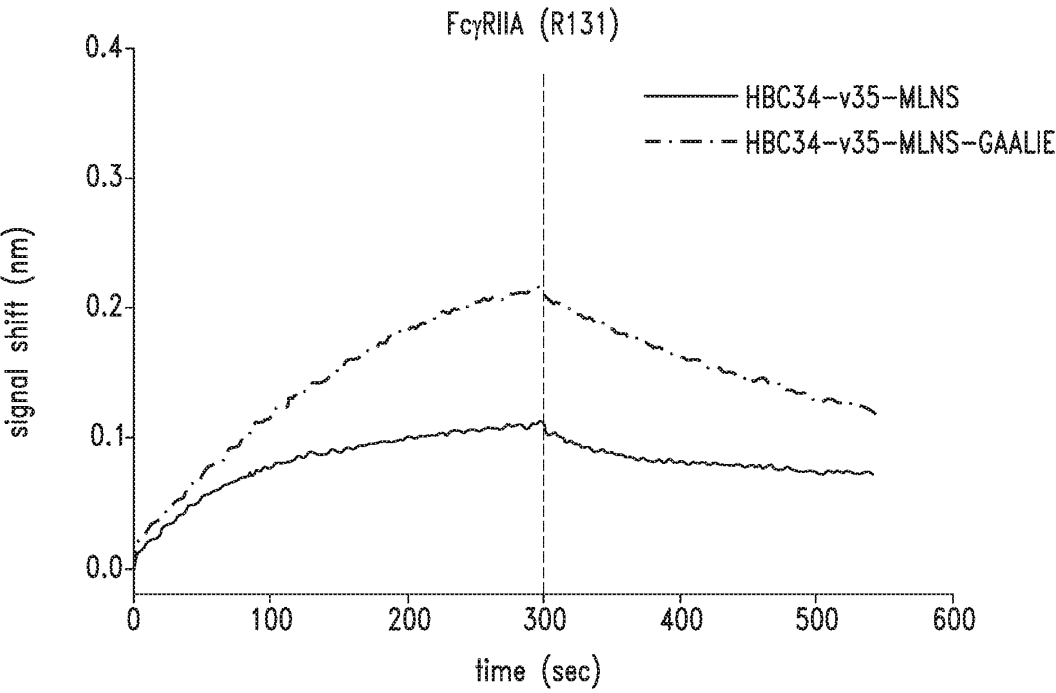


FIG. 8B

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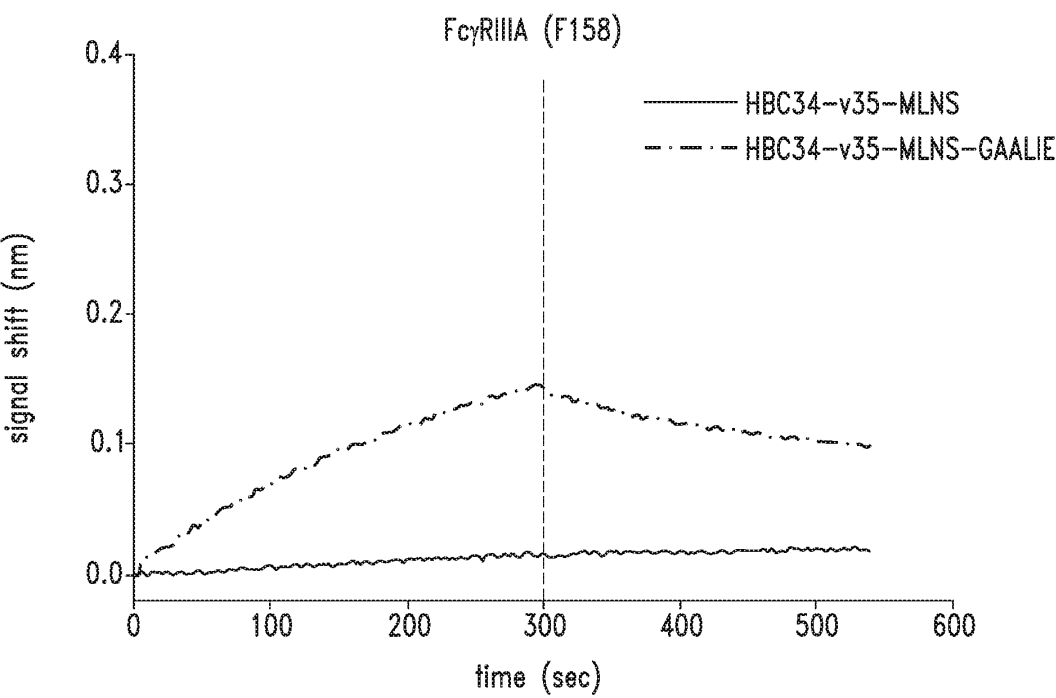


FIG. 8C

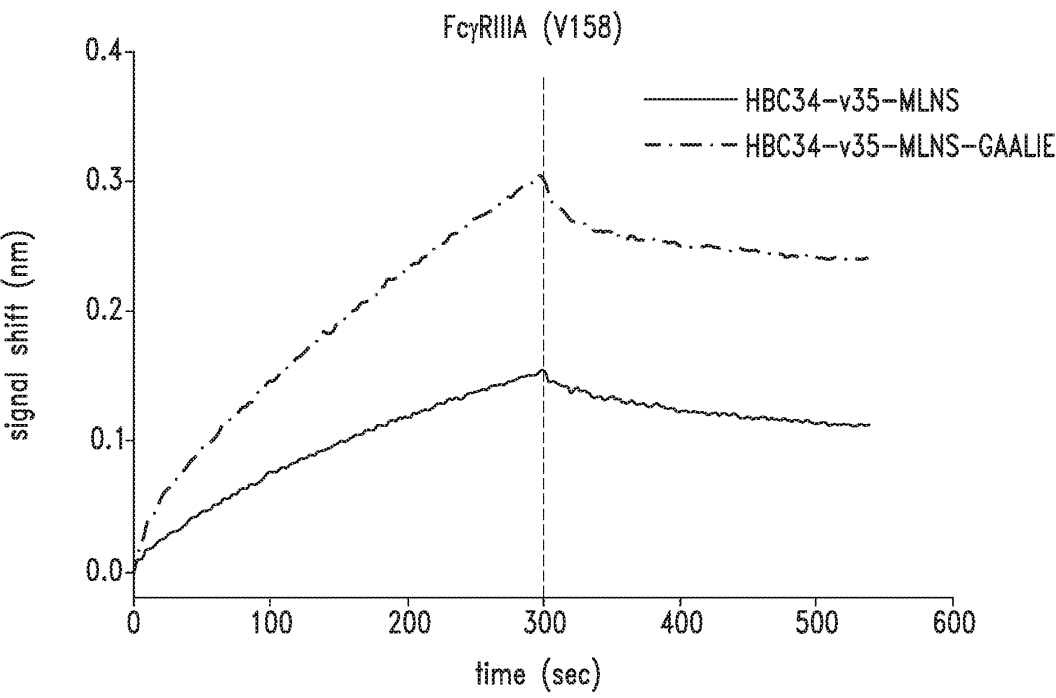
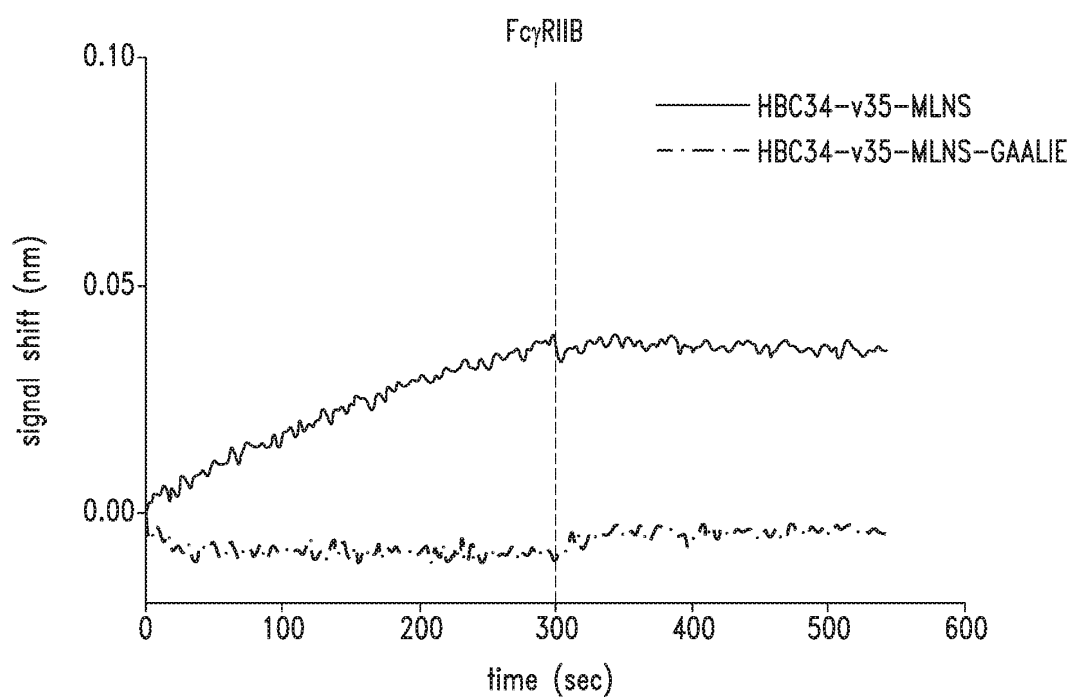
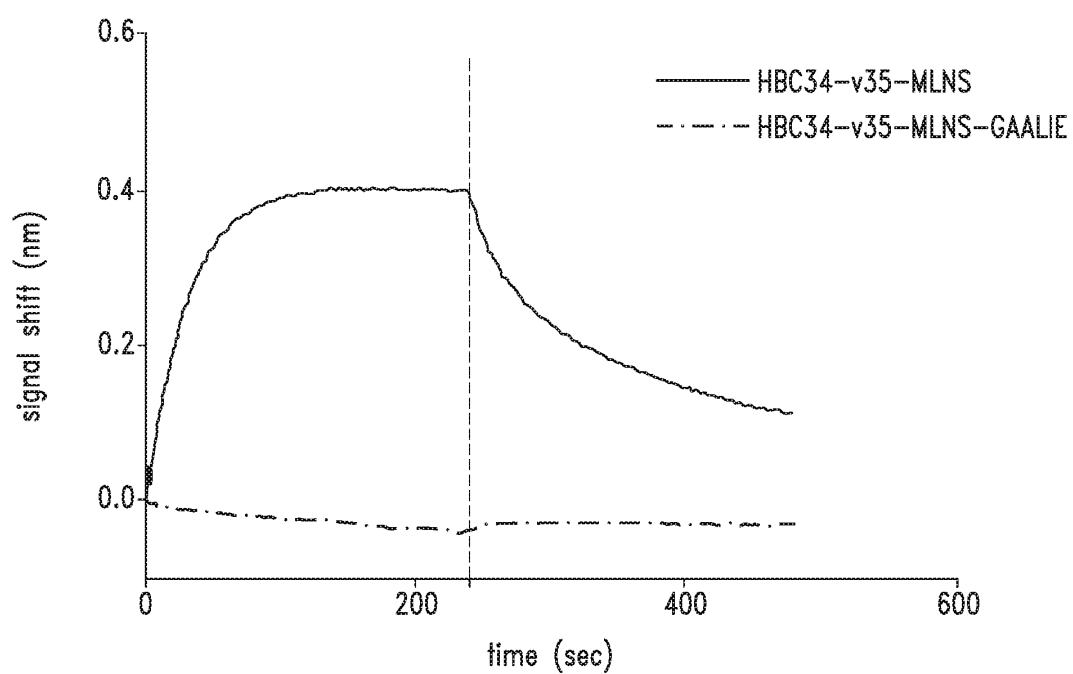


FIG. 8D

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*FIG. 8E**FIG. 9*

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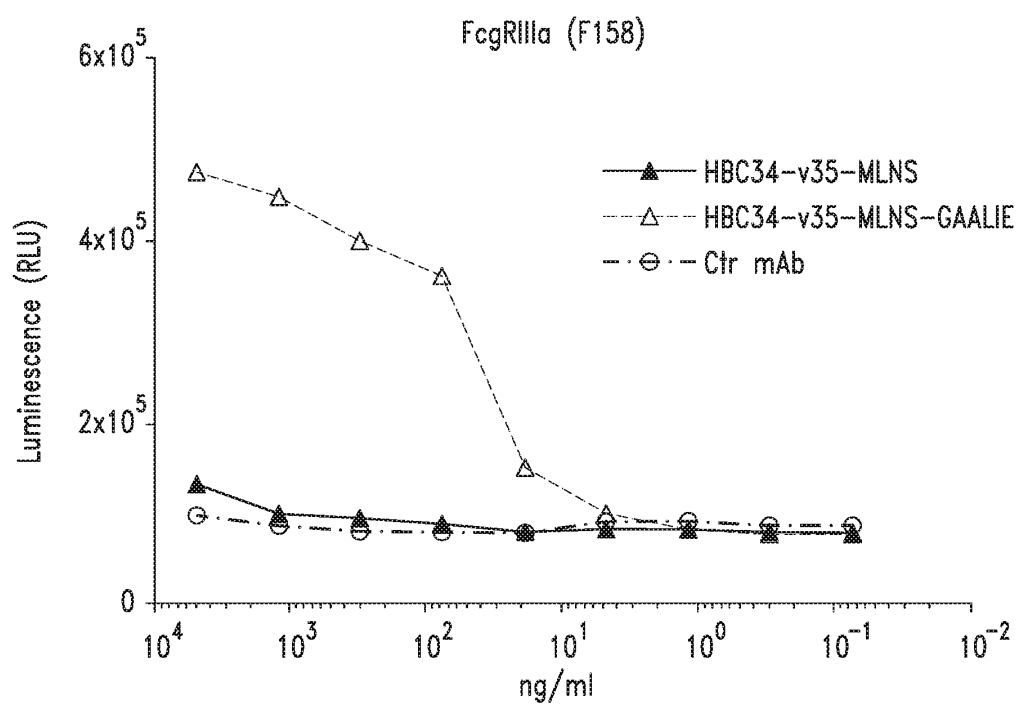


FIG. 10A

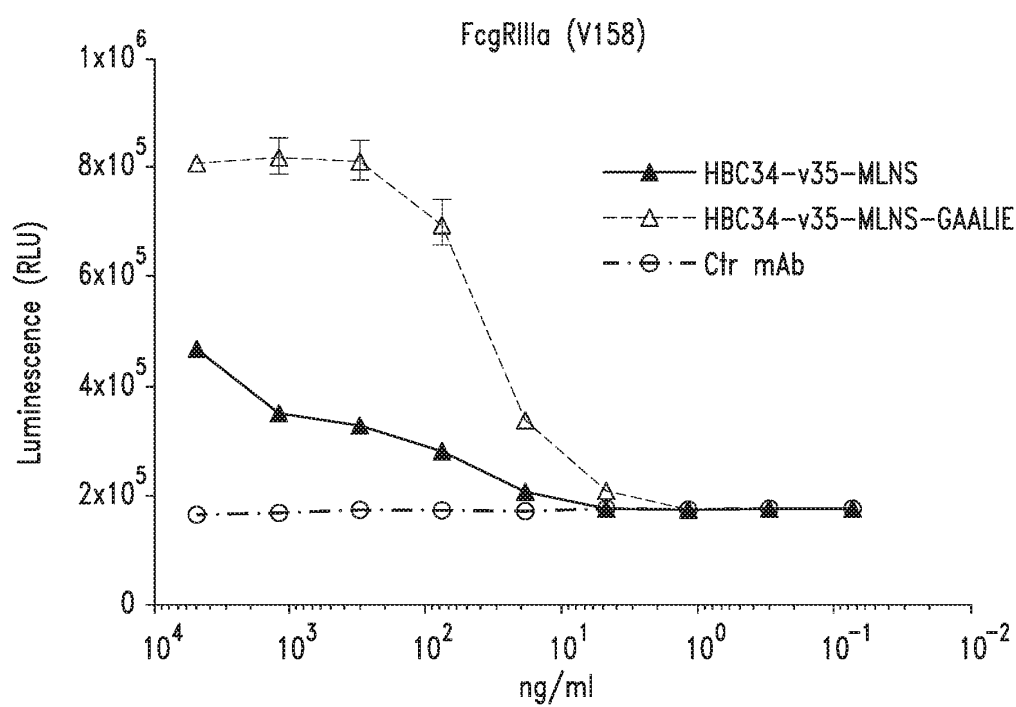


FIG. 10B

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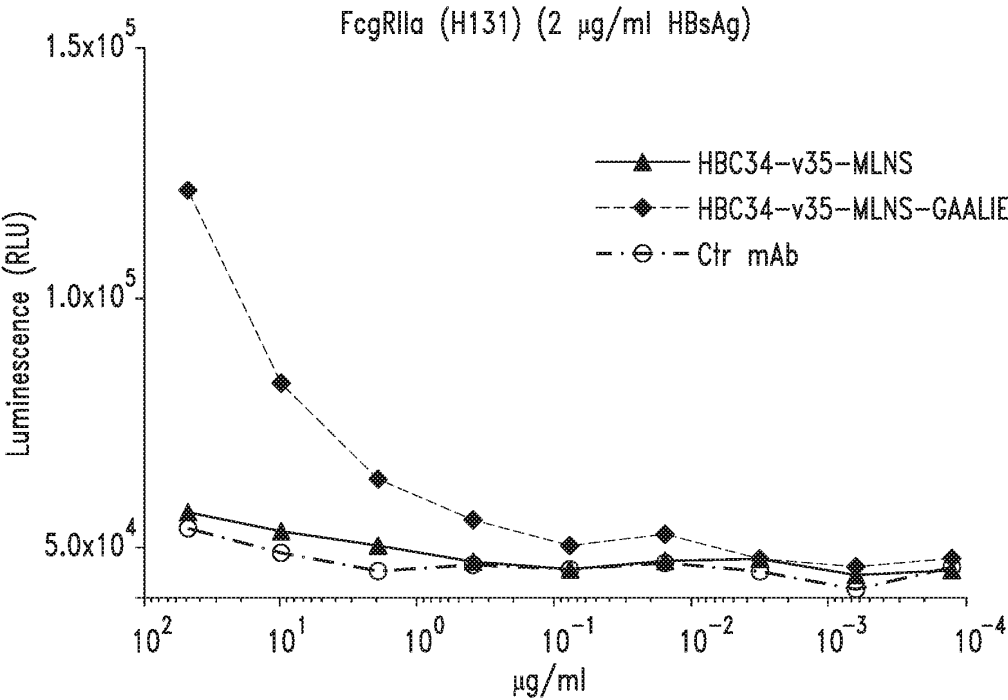


FIG. 11A

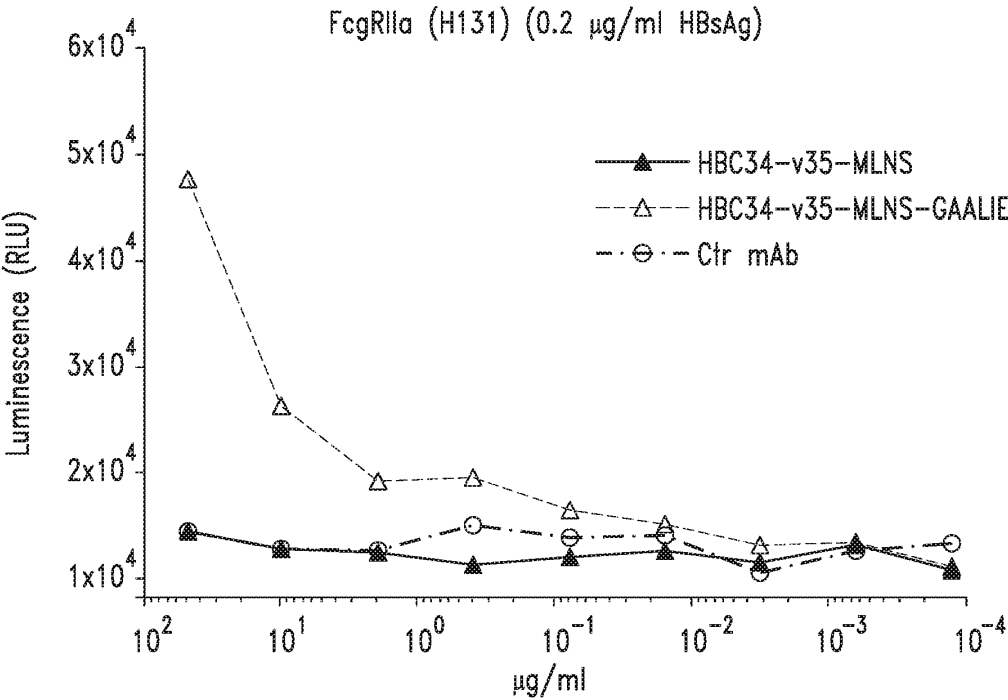


FIG. 11B

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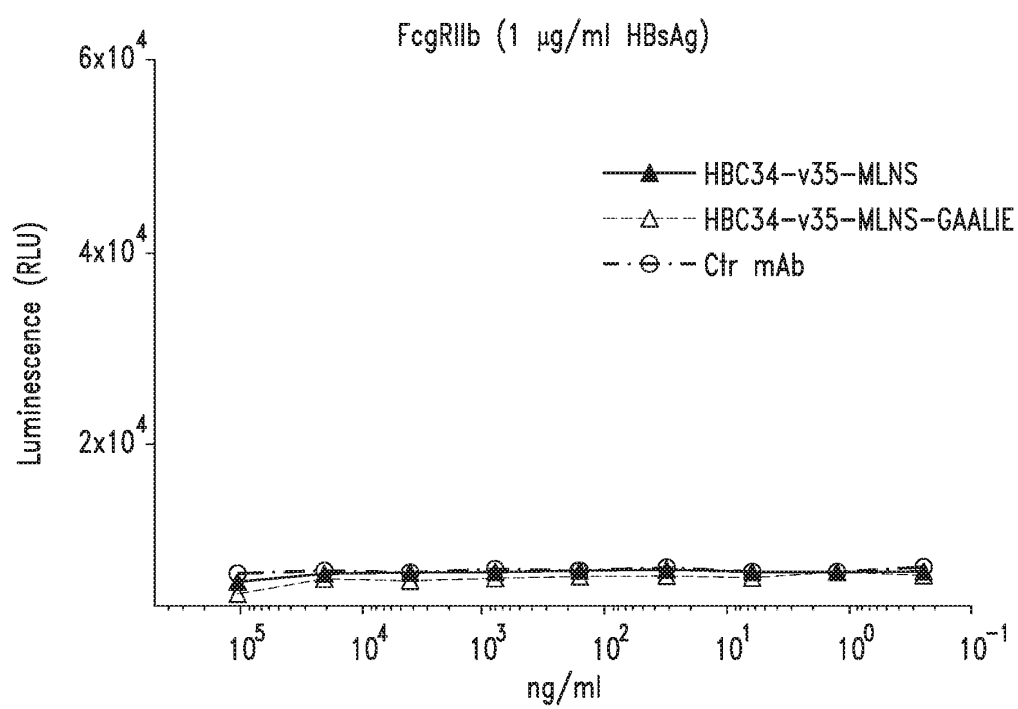


FIG. 12

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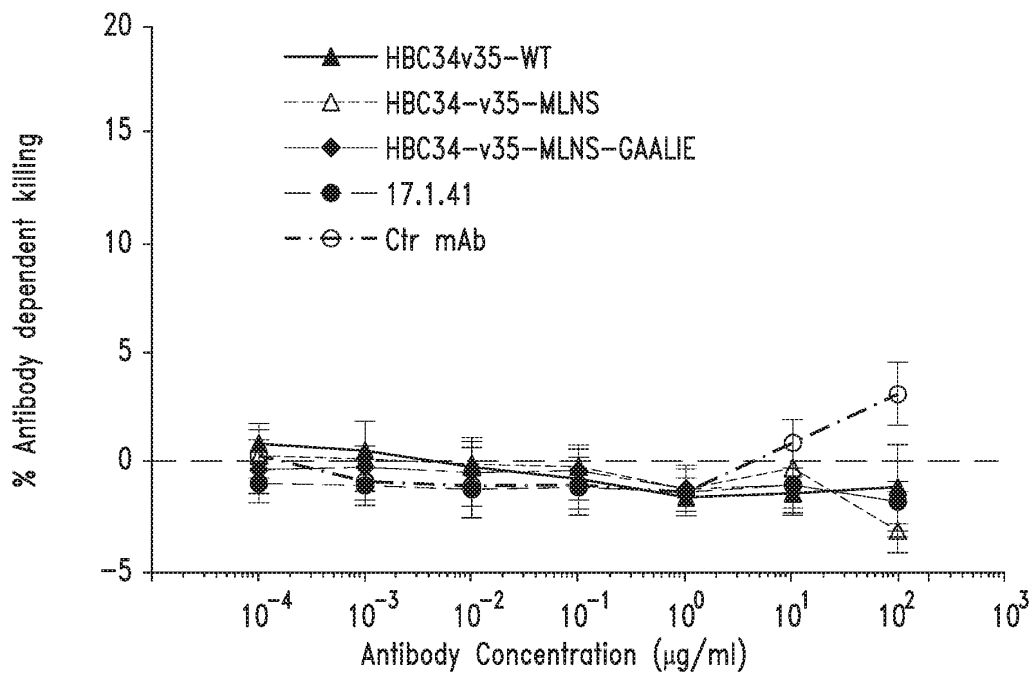


FIG. 13A

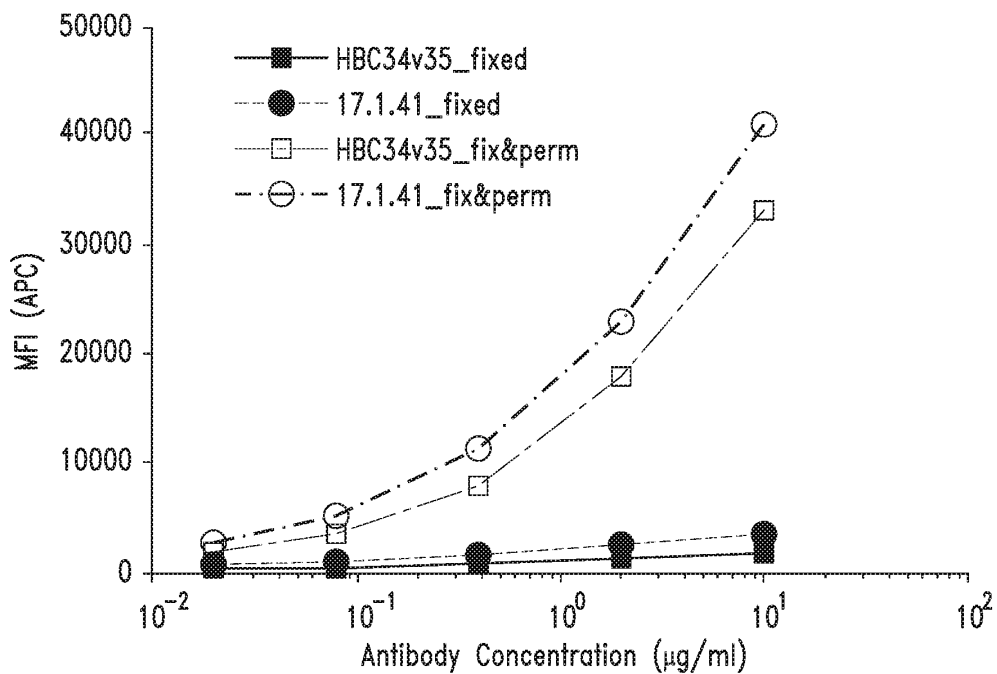


FIG. 13B

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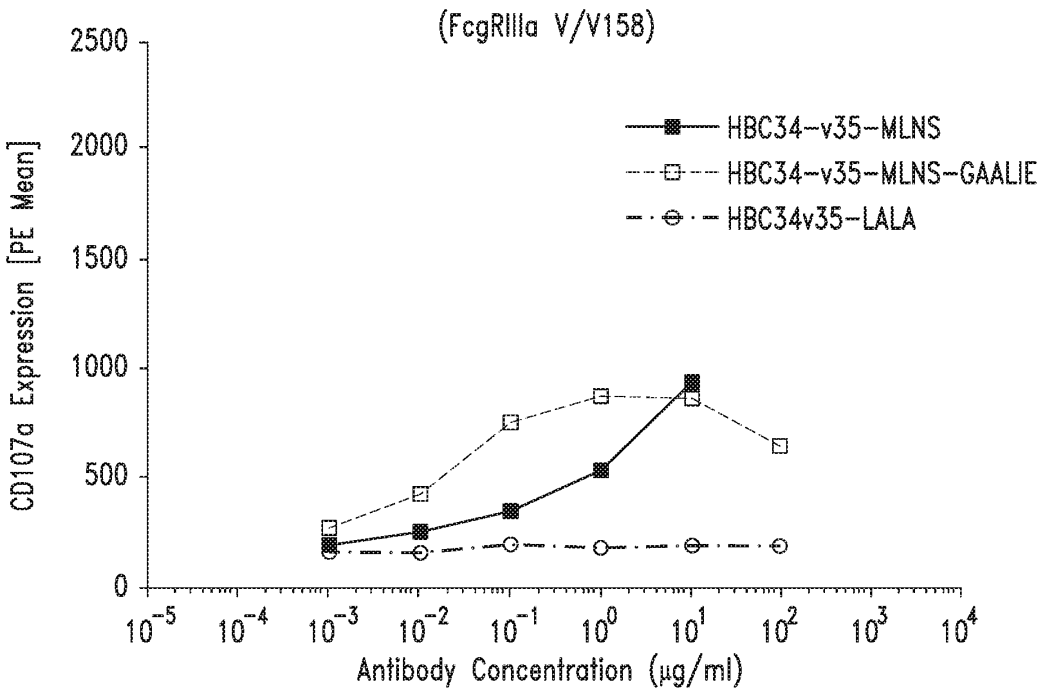


FIG. 14A

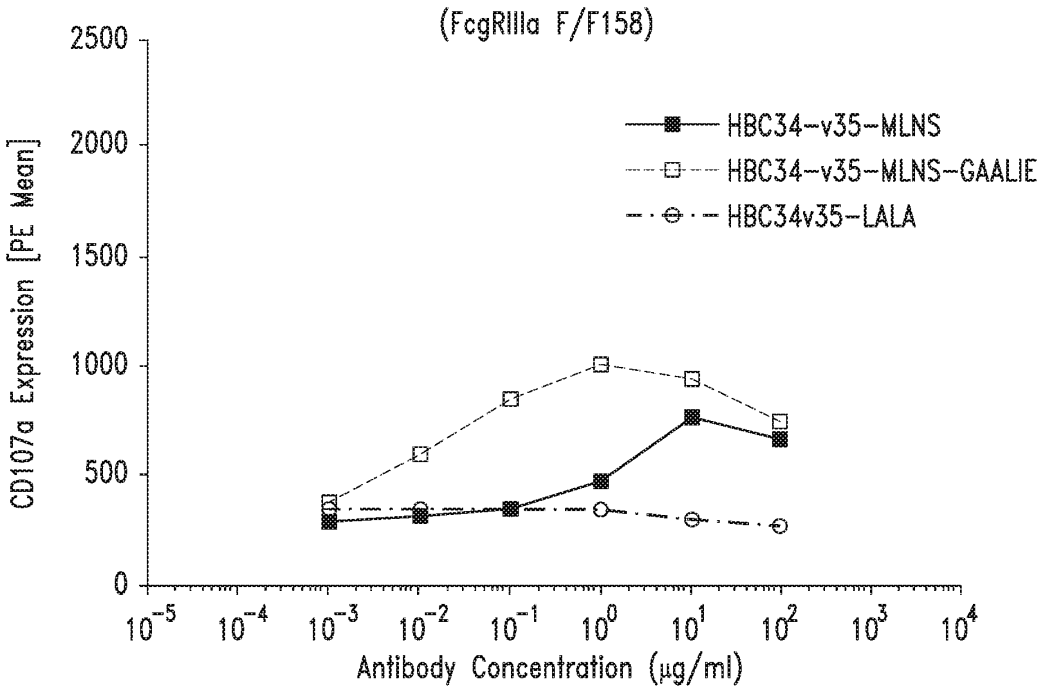


FIG. 14B

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Part A													
Inpatient ^a			Outpatient										
Study Stage	Screening	Dosing Day	Post-dose Follow-up Period										
			W1	W2	W4	W8	W12	W18	W24/E18				
Study Visit Week													
Study Visit Day±Visit Window	D -28 to -1	D1 ^c	D2	D4±1	D8±1	D15±2	D29±2	D57±7	D85±7	D127±7	D169±7		
Informed consent	X												
Demography	X												
Medical history ^d	X												
Inclusion/exclusion criteria	X	X ^e											
Full physical examination ^f	X												X
Symptom-directed physical examination		X	X	X	X		X	X	X	X			
Body weight	X												
Height	X												
Vital signs ^g	X	X	X	X	X	X	X	X	X	X	X	X	X
Safety ECGs ^h	X	X	X	X	X								
Pregnancy test ⁱ	X	X					X	X	X	X	X	X	X
Screening viral serology ^j	X												
Liver Function Tests ^k	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum Chemistry ^l	X	X	X	X	X	X	X	X	X	X	X	X	X

FIG. 15A

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Part A												
Study Stage	Inpatient ^a		Outpatient									
	Screening	Dosing Day	Post-dose Follow-up Period									
Study Visit Week												
Study Visit Day ± Visit Window	D -28 to -1	D1 ^c	D2	D4 ± 1	D8 ± 1	W1	W2	W4	W8	W12	W18	W24/EI ^b
Hematology ^a	X	X	X	X	X	X	X	X	X	X	X	X
Coagulation Parameters ^a	X	X			X	X		X	X	X		X
Urinalysis ^a	X											
Urine for drugs of abuse ^c	X	X										
Randomization		X										
Study drug administration ^a		X										
Blood samples for PK analysis ^d		X	X	X	X	X	X	X	X	X	X	X
Blood samples for immunogenicity analysis ^e		X					X	X	X	X	X	X
Local tolerability ^f		X	X	X	X							
Review/record AEs ^g												
Concomitant medications												

AE = adverse event; ECG = electrocardiogram; EI = end of treatment; PK = pharmacokinetic; SAD = single ascending dose

Note: When scheduled at the same timepoints, the assessments of vital signs and 12-lead ECGs must be performed before the blood sample collections.

^a Subjects may be admitted to the clinical investigative site on Day -1 or Day 1 and will be discharged following the completion of the Day 2 assessments.

^b If a subject withdraws prematurely from the study prior to the Week 24 visit, Week 24/EI assessments should be performed.

^c Assessments performed predose unless otherwise specified.

^d Complete medical history will be taken at screening and any changes should be updated prior to dosing.

^e Evaluation of specified inclusion and exclusion criteria.

^f A full physical examination will include general appearance, head, neck, chest/respiratory, heart/cardiopulmonary, gastrointestinal/liver, extremities, skin, and screening neurological assessments.

FIG. 15B

- 2 Vital signs (blood pressure, pulse rate, respiratory rate and temperature) should be measured after the subject has rested comfortably for approximately 10 minutes. On Day 1, vital signs should be measured within 2 hours prior to dose and at 2 hours (+/- 1 hour) post-dose (SC administration only) or 2 hours (+/- 1 hour) post-end of infusion (IV administration only). On all other visit days, vital signs are only required to be recorded once during the visit.
- 3 All ECGs should be measured in the supine position after the subject has rested comfortably for approximately 10 minutes. On Day 1, 12-lead safety ECGs will be recorded predose (within 30 minutes prior to dose) and at 2 hours (+/- 1 hour) post-dose (SC administration only) or 2 hours (+/- 1 hour) post-end of infusion (IV administration only). Additionally, ECGs on Day 4 and Day 8 only need to be collected for subjects receiving study drug by SC administration. WOCBP are required to have pregnancy tests. A blood pregnancy test will be performed at screening and a urine pregnancy test will be performed thereafter. The pregnancy test scheduled for Day 1 may be performed on Day -1 per local practices. Negative pregnancy test must be confirmed prior to study drug administration.
- 4 Viral serology parameters are described in Example 9.
- 5 Clinical laboratory and urinalysis parameters are as described in Example 9.
- 6 Drugs of abuse included in the screen are described in Example 9. Collection of urine for drugs of abuse scheduled for Day 1 may be performed on Day -1 per local practices. Results for drugs of abuse must be reviewed prior to dosing. Local drugs of abuse assessment will be confirmed by central testing.
- 7 Study drug will be administered via IV infusion or SC injection as described in Example 9.
- 8 On Day 1, for subjects receiving study drug by SC injection, blood samples for PK analysis will be collected predose and at 1 hour, 4 hours, and 8 hours post-dose. On Day 1, for subjects receiving study drug by IV infusion, blood samples for PK analysis will be collected predose, at end of infusion, and 1, 4 and 8 hours post end of infusion.
- 9 Includes samples for ADA and neutralizing antibodies (NAb), as applicable. Additional unscheduled samples for immunogenicity analysis may be collected if an immunologic related event is suspected. Immunogenicity sampling beyond the planned follow-up period may occur based on emerging results.
- 10 Local tolerability only needs to be assessed for subjects who are administered study drug by SC injection. On Day 1, local tolerability should be assessed at approximately 1 hour post-dose. At the discretion of the investigator, unscheduled visits are permitted as needed for follow up of any unresolved local tolerability symptoms.
- 11 All AEs related to screening activities must be collected starting at the time of consent; any other events occurring during the screening period should be reported as medical history. All SAEs must be collected from the time of consent onwards.

FIG. 15C

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Part B/C														
Study Stage	Screening	Inpatient ^a		Outpatient										
		Dosing Day	Post-dose Follow-up Period					Extended Follow-up Period ^b						
Study Visit Week			W1	W2	W4	W8/ET ^c	W12	W16	W24	W32	W40 / EF ^d			
Study Visit Day $\pm$ Visit Window	D -28 to -1	D1 ^e	D2	D4+1	D8 $\pm$ 1	D11 $\pm$ 1	D15 $\pm$ 2	D19 $\pm$ 2	D57 $\pm$ 7	D85 $\pm$ 7	D113 $\pm$ 7	D169 $\pm$ 7	D225 $\pm$ 7	D281 $\pm$ 7
Informed consent	X													
Demography	X													
Medical history including HBV genotype ^f	X													
Inclusion/exclusion criteria	X	X ^g												
Full physical examination ^h	X		X						X					
Symptom-directed physical examination		X	X		X		X	X						
Body weight	X													
Height	X													
Vital signs ⁱ	X	X	X	X	X		X	X	X					
Safety ECG ^j	X													
Pregnancy test ^k	X	X							X	X	X	X	X	X
FibroScan ^l	X													
Screening viral serology ^m	X													

FIG. 16A

Part B-C													
Study Stage	Inpatient ^a			Outpatient									
	Screening	Dosing Day	Post-dose Follow-up Period					Extended Follow-up Period ^b					
Study Visit Week				W1	D11±1	W2	W4	W8/ET ^c	W12	W16	W24	W32	W40 / EF ^c
Study Visit Day=Visit Window	D -28 to -1	D1 ^e	D2	D4+1	D8±1	D15±2	D29±2	D57±7	D85 ±7	D113 ±7	D169 ±7	D225 ±7	D281 ±7
Liver Function Tests ^d	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum Chemistry ^d	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology ^d	X	X	X	X	X	X	X	X					
Coagulation Parameters ^d	X	X	X	X	X	X	X	X					
Complement testing ^d		X			X	X							
Urinalysis ^{d,e}	X	X			X	X							
Urine for drugs of abuse ^d	X												
Study drug administration ^f		X											
Blood samples for PK analysis ^f		X	X	X	X	X	X	X	X	X	X	X	X
Blood samples for immunogenicity analysis ^f		X				X	X	X	X	X	X	X	X
Blood sample for quantitative HBsAg	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood sample for anti-HBs	X				X	X	X	X	X	X	X	X	X
Blood sample for HBcAg qualitative	X							X ^g					X ^g
Blood sample for HBcAg quantitative ^g		X					X	X					X

FIG. 16B

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Part B/C														
Study Stage	Screening	Dosing Day	Inpatient ^a		Outpatient									
			Post-dose Follow-up Period					Extended Follow-up Period ^b						
Study Visit Week					W1		W2	W4	W8/ET ^c	W12	W16	W24	W32	W40 / EF ^a
Study Visit Day $\pm$ Visit Window	D -28 to -1	D1 ^a	D2	D4+1	D8 $\pm$ 1	D11 $\pm$ 1	D15 $\pm$ 2	D29 $\pm$ 2	D57 $\pm$ 7	D85 $\pm$ 7	D113 $\pm$ 7	D169 $\pm$ 7	D225 $\pm$ 7	D281 $\pm$ 7
Blood sample for anti-HBe		X							X					X
Blood sample for HBV RNA quantitation and HBcrAg quantitation		X						X	X	X		X	X	X
Blood sample for HBV DNA quantitation ^a	X	X			X		X	X	X	X		X		X
Blood sample for analysis of immune responses ^a		X			X		X	X	X	X		X		X
Hepatic fine-needle aspirate sample collection ^a		X					X	X	X					
Blood sample for RNA Paxgene tube ^a		X			X		X	X	X	X		X		X
HBV resistance surveillance ^{a,v}		X			X		X	X	X	X		X	X	X
Blood sample for Fc gamma receptor genotyping and for immunoglobulin allotyping		X												
Local tolerability ^a		X	X	X	X									
Review/record AEs ^a			X					X					X	
Concomitant medications			X											

FIG. 16C

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Part B/C														
Study Stage	Inpatient ^a			Outpatient										
	Screening	Dosing Day	Post-dose Follow-up Period							Extended Follow-up Period ^b				
			W1		W2	W4	W8/ET ^c	W12	W16	W24	W32	W40 / EF ^d		
Study Visit Week														
Study Visit Day±Visit Window	D -28 to -1	D1 ^e	D2	D4+1	D8±1	D11±1	D15±2	D29±2	D57±7	D85 ±7	D113 ±7	D169 ±7	D225 ±7	
NRTI medication adherence ^g	X													

AE = adverse event; ECG = electrocardiogram; EF = end of follow-up; ET = end of treatment; HBcrAg = hepatitis B core-related antigen; HBsAg = hepatitis B e-antigen; HBsAg = hepatitis B surface antigen; HBV = Hepatitis B Virus; NRTI = nucleoside/nucleotide reverse transcriptase inhibitor; PK = pharmacokinetic; SAD = single ascending dose

Note: When scheduled at the same timepoints, the assessments of vital signs and 12-lead ECGs must be performed before the blood sample collections.

^a Subjects will be admitted to the clinical investigative site on Day -1 or 1 and discharged following the completion of the Day 2 assessments.

^b Following Week 8, subjects with > 2 -fold HBsAg reduction at Week 8 should be followed for up to 40 weeks or until the reduction in HBsAg is < 2 -fold relative to baseline at 2 consecutive collections, whichever occurs first. The extended follow-up may be discontinued at the Sponsor's discretion based on emerging data.

^c If a subject withdraws participation prematurely from the study prior to the Week 8 visit, Week 8 ET assessments should be performed.

^d If a subject withdraws participation prematurely from the study after the Week 8 visit and prior to the Week 40 visit, Week 40 EF assessments should be performed.

^e Assessments performed predose unless otherwise specified.

^f A complete medical history will be taken at screening including HBV genotype if available. Any changes should be updated prior to dosing.

^g Evaluation of specified inclusion and exclusion criteria. See Example 9 for more information.

^h See Example 9 for assessments to be performed during a full physical examination.

ⁱ Vital signs (blood pressure, pulse rate, respiratory rate and temperature) should be measured after the subject has rested comfortably for approximately 10 minutes. On Day 1, vital signs should be measured within 2 hours prior to dose and at 2 hours post-dose ($\pm$ 1 hour). On all other visit days, vital signs are only required to be recorded once during the visit.

^j ECGs should be measured in the supine position after the subject has rested comfortably for approximately 10 minutes.

^k WOCBP are required to have pregnancy tests. A blood pregnancy test will be performed at screening and a urine pregnancy test will be performed thereafter. Negative pregnancy test must be confirmed prior to study drug administration.

^l Does not need to be performed if the subject has had a FibroScan in the 6 months prior to screening or liver biopsy in the year prior to screening that confirmed the absence of Metavir F3 fibrosis or F4 cirrhosis.

^m See Example 9 for viral serology parameters.

FIG. 16D

- * Clinical laboratory and urinalysis parameters are described in Example 9. For subjects and days in which hepatic fine-needle aspirate samples are collected, safety laboratory assessments (liver function tests, serum chemistry, hematology, and coagulation parameters) should be collected prior to hepatic fine-needle aspirate sample collection.
- * Additional samples may be collected at any time post-dosing if immune-complex disease is suspected.
- * Drugs of abuse included in the screen are described in Example 9.
- * Study drug will be administered via SC injection as described in Example 9.
- * On Day 1, blood samples for PK analysis will be collected predose and at 1 hour, 4 hours, and 8 hours post-dose. Includes samples for free and total PK assays.
- * Includes samples for ADA and neutralizing antibodies (NAb), as applicable. Additional unscheduled samples for immunogenicity analysis may be collected if an immunologic related event is suspected. Immunogenicity sampling beyond the planned follow-up period may occur based on emerging results. Further details can be found in Example 9.
- * Should only be collected for Part C subjects who are HBeAg qualitative positive at screening.
- * If a subject experiences ALT flare (as defined by >2-fold increase in ALT relative to Day 1 predose ALT), additional HBV DNA quantitation and HBV resistance surveillance sample(s) may be collected.
- * See the Laboratory Manual for instructions on sample processing and aliquoting for storage and potential immune-related exploratory analyses. Blood samples only need to be collected when and where available at select sites as an optional sub-study. As these assessments are exploratory, the collection and specific assays used may be changed or removed at the Sponsor's discretion based on emerging data. Further details can be found in Example 9.
- * See the Laboratory Manual for instructions on collection and processing of hepatic fine-needle aspirate samples. Samples only need to be collected when and where available at select sites as an optional sub-study. As these assessments are exploratory, the collection and specific assays used may be changed or removed at the Sponsor's discretion based on emerging data. Further details can be found in Example 9.
- * As this assessment is exploratory, the collection and specific assays used may be changed or removed at the Sponsor's discretion based on emerging data. Further details can be found in Example 9.
- * See Example 9 for more information.
- * On Day 1, local tolerability should be assessed at approximately 1 hour post-dose. At the discretion of the investigator, unscheduled visits are permitted as needed for follow up of any unresolved local tolerability symptoms.
- ** All AEs related to screening activities must be collected starting at the time of consent; any other events occurring during the screening period should be reported as medical history. All SAEs must be collected from the time of consent onwards. All AEs will be collected through the Week 8/EI visit. Following Week 8, only targeted AEs and SAEs need to be collected through the end of the study. Further details can be found in Example 9.
- ** NRTIs will be continued through the end of follow-up for each subject.

FIG. 16E

PART A PHARMACOKINETIC TIMEPOINTS (SC INJECTION)

Study Day ± window in days (Study Week)	Protocol Time	Blood PK (serum)
Day 1	Predose	X
	Dose	
	1 hour	X
	4 hours	X
	8 hours	X
Day 2	24 hours	X
Day 4 ± 1		X
Day 8 ± 1 (Week 1)		X
Day 15 ± 2 (Week 2)		X
Day 29 ± 2 (Week 4)		X
Day 57 ± 7 (Week 8)		X
Day 85 ± 7 (Week 12)		X
Day 127 ± 7 (Week 18)		X
Day 169 ± 7 (Week 24)		X

FIG. 17A

PART A PHARMACOKINETIC TIMEPOINTS (IV INFUSION)

Study Day + window in days (Study Week)	Protocol Time	Blood PK (serum)
Day 1	Predose	X
	Dose	
	End of infusion	X
	1 hour post-end of infusion	X
	4 hours post-end of infusion	X
	8 hours post-end of infusion	X
Day 2	24 hours post-end of infusion	X
Day 4 ± 1		X
Day 8 ± 1 (Week 1)		X
Day 15 ± 2 (Week 2)		X
Day 29 ± 2 (Week 4)		X
Day 57 ± 7 (Week 8)		X
Day 85 ± 7 (Week 12)		X
Day 127 ± 7 (Week 18)		X
Day 169 ± 7 (Week 24)		X

FIG. 17B

PARTS B/C PHARMACOKINETIC TIMEPOINTS

Study Day $\pm$ window in days (Study Week)	Protocol Time	Blood PK (serum)
Day 1	Predose	X
	Dose	
	1 hour	X
	4 hours	X
	8 hours	X
Day 2	24 hours	X
Day 4 $\pm$ 1		X
Day 8 $\pm$ 1 (Week 1)		X
Day 11 $\pm$ 1		X
Day 15 $\pm$ 2 (Week 2)		X
Day 29 $\pm$ 2 (Week 4)		X
Day 57 $\pm$ 7 (Week 8)		X
Day 85 $\pm$ 7 (Week 12)		X
Day 113 $\pm$ 7 (Week 16)		X
Day 169 $\pm$ 7 (Week 24)		X
Day 225 $\pm$ 7 (Week 32)		X
Day 281 $\pm$ 7 (Week 40)		X

FIG. 17C

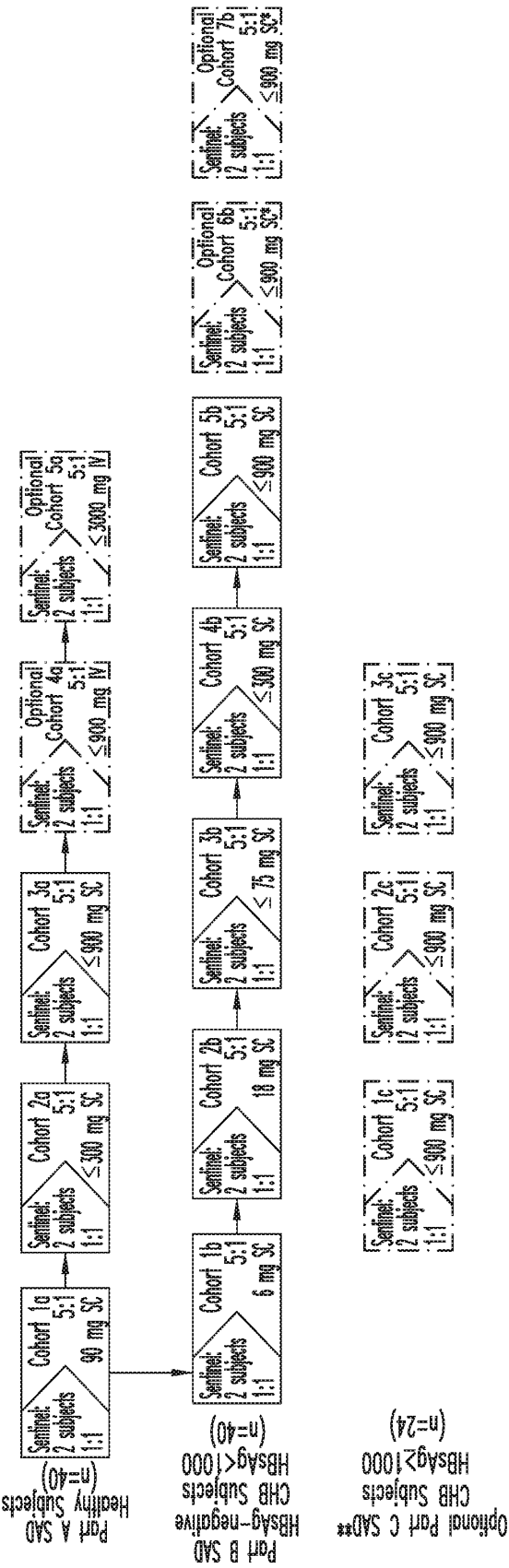


FIG. 18

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Hematology	
Alanine aminotransferase (ALT)	Bilirubin (total and direct)
Coagulation Parameters	
International normalized ratio (INR) time	Prothrombin
Urinalysis	
Bilirubin	Proteins
Glucose	Red blood cells (RBCs)
Ketones	Screen for drugs of abuse
Leukocytes	Specific gravity
Microscopy (if clinically indicated)	Urobilinogen
Nitrite	Visual inspection for appearance and color
pH	
Pregnancy Testing	
Beta-human chorionic gonadotropin (WOCBP only)	Urine pregnancy test
Screening Viral Serology	
Hepatitis B, C ^a , and Delta	Human immunodeficiency virus I and II

^aOnly required if ALT and/or AST is elevated >2x the predose Day 1 baseline value^bSubjects in Part B/C with positive HCV screening serology may have HCV RT-PCR performed to determine eligibility

FIG. 19

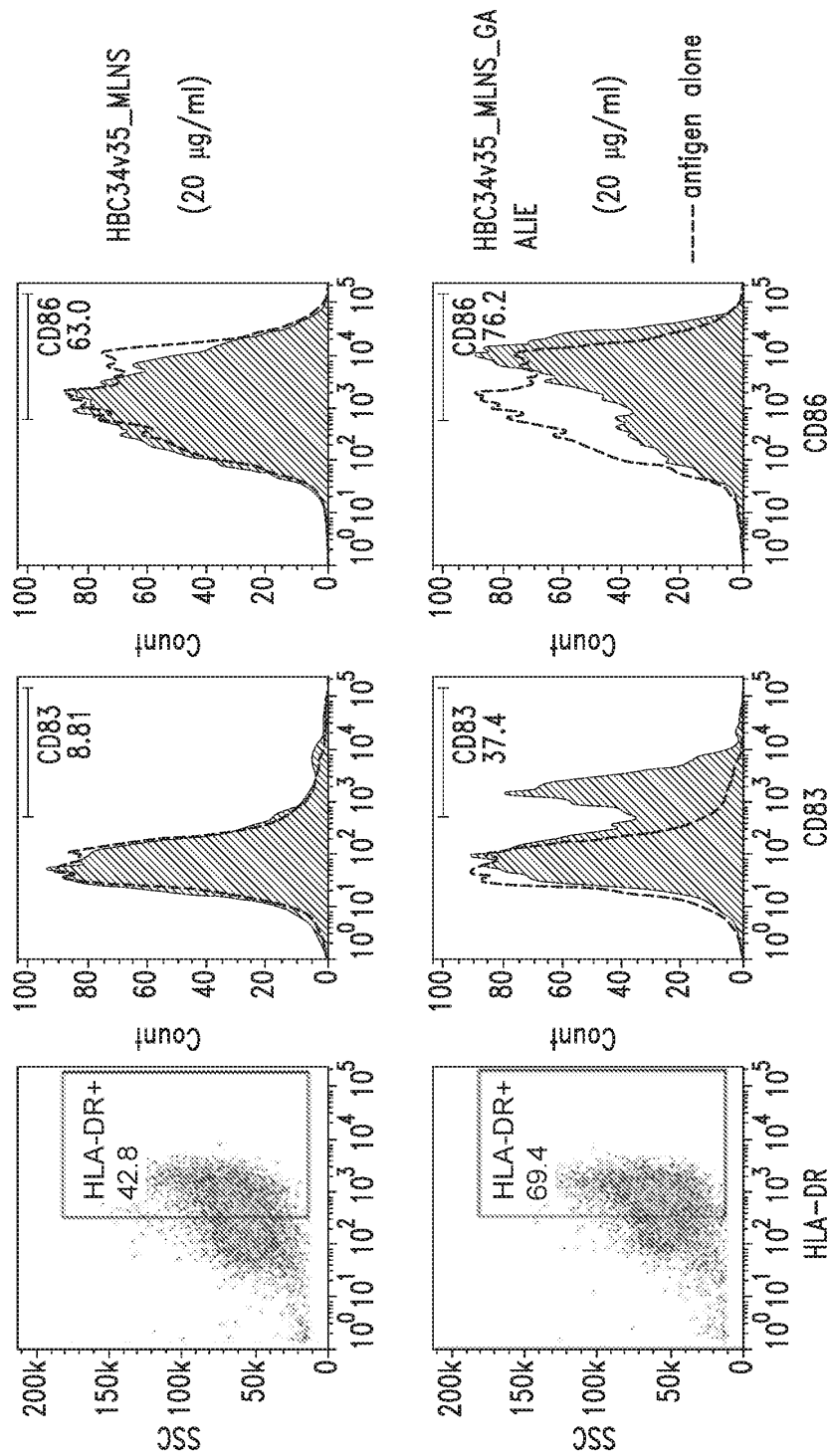


FIG. 20

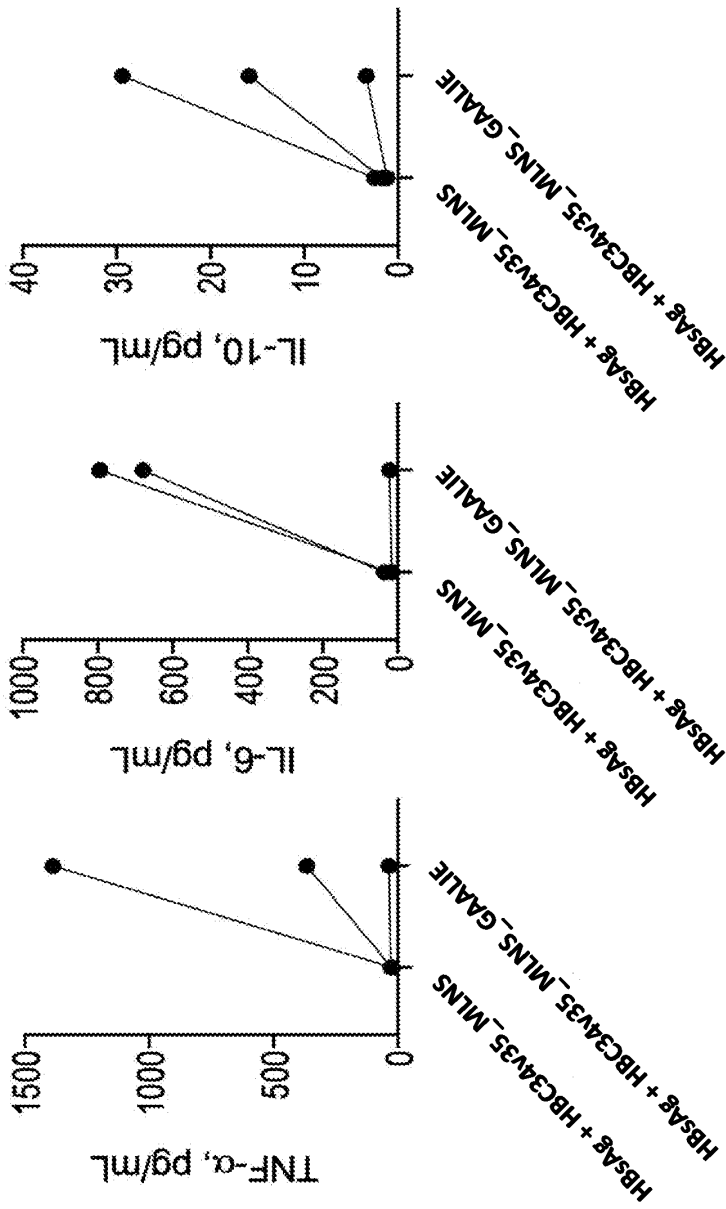


FIG. 21

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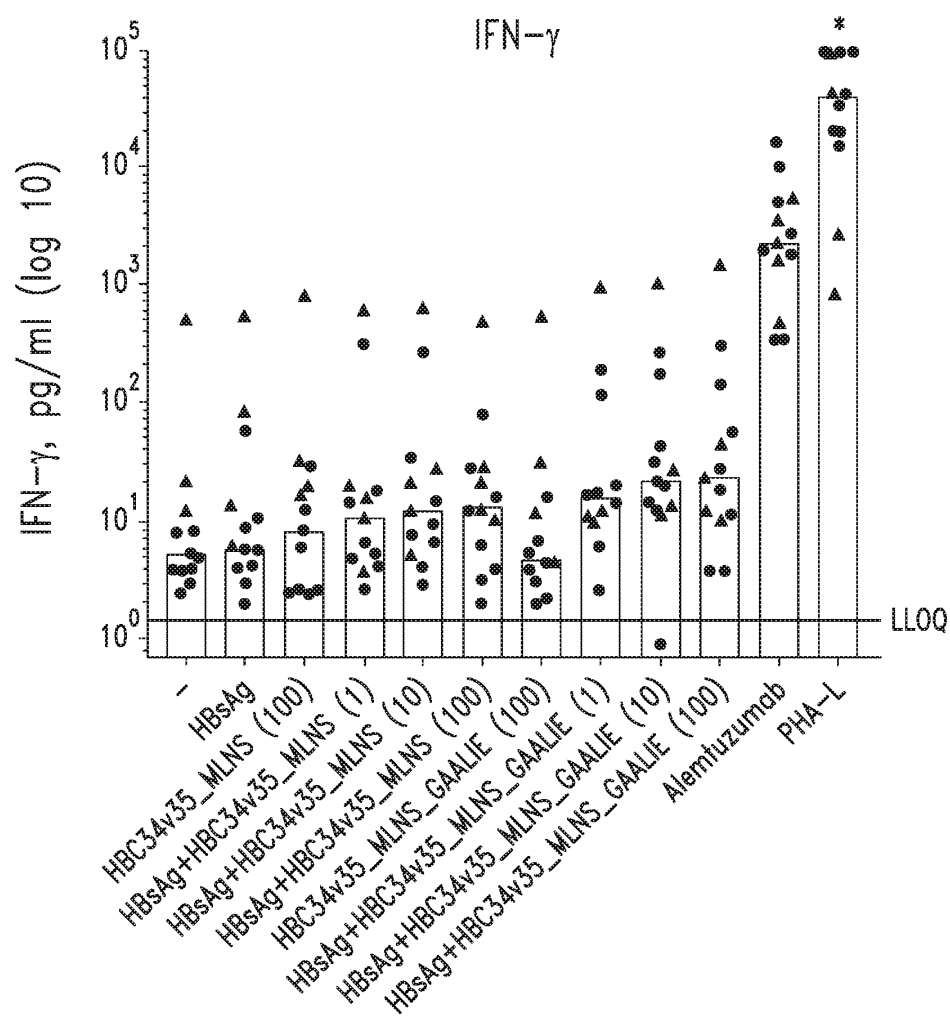


FIG. 22A

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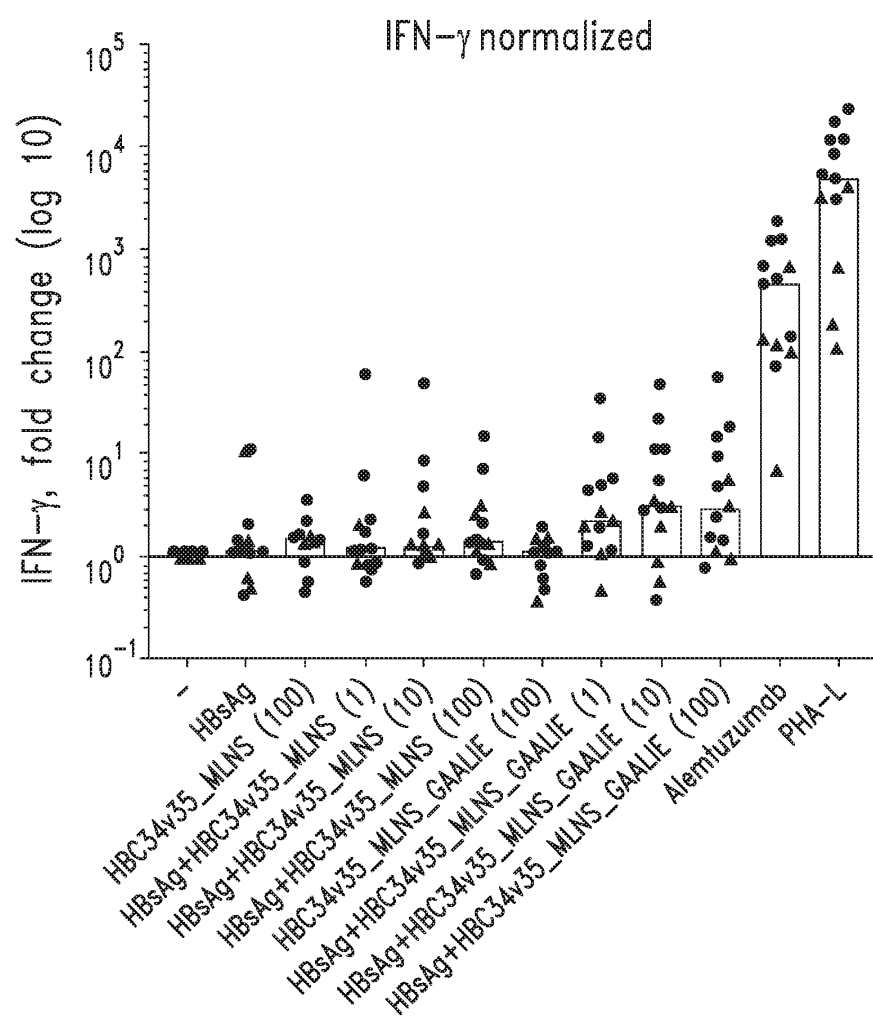


FIG. 22B

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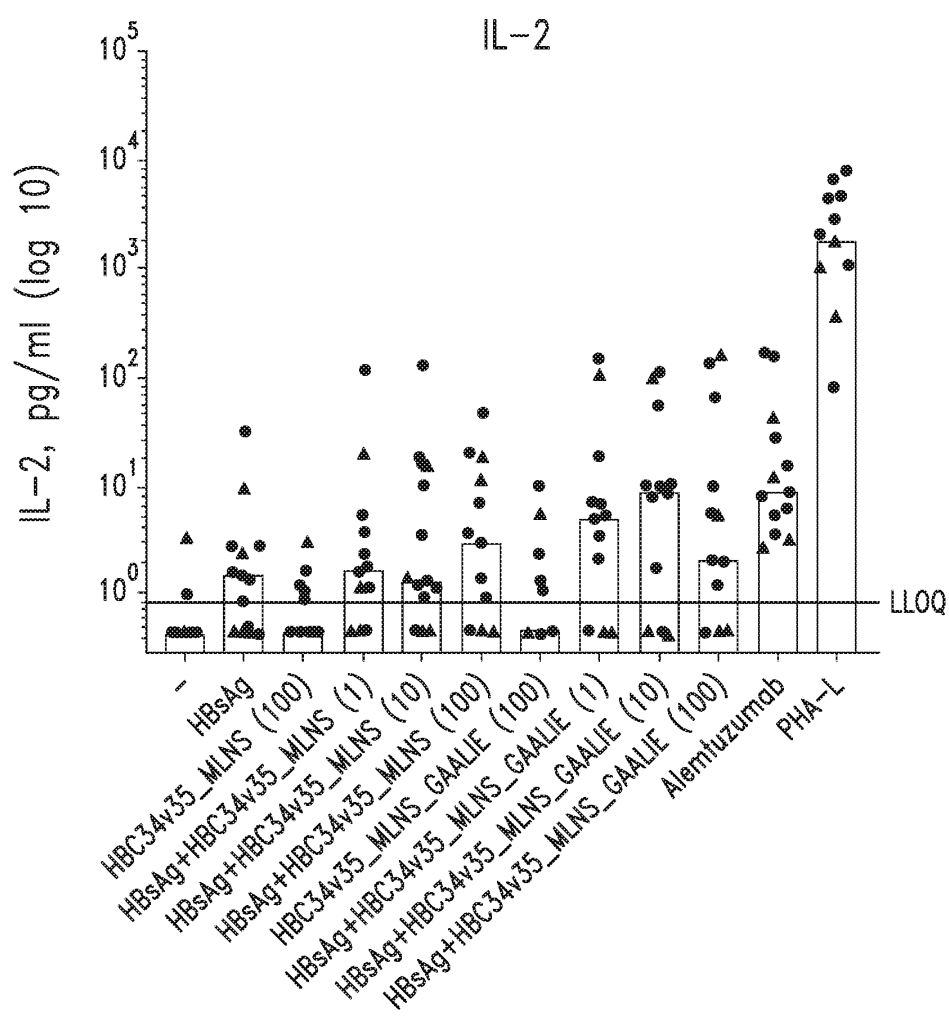


FIG. 23A

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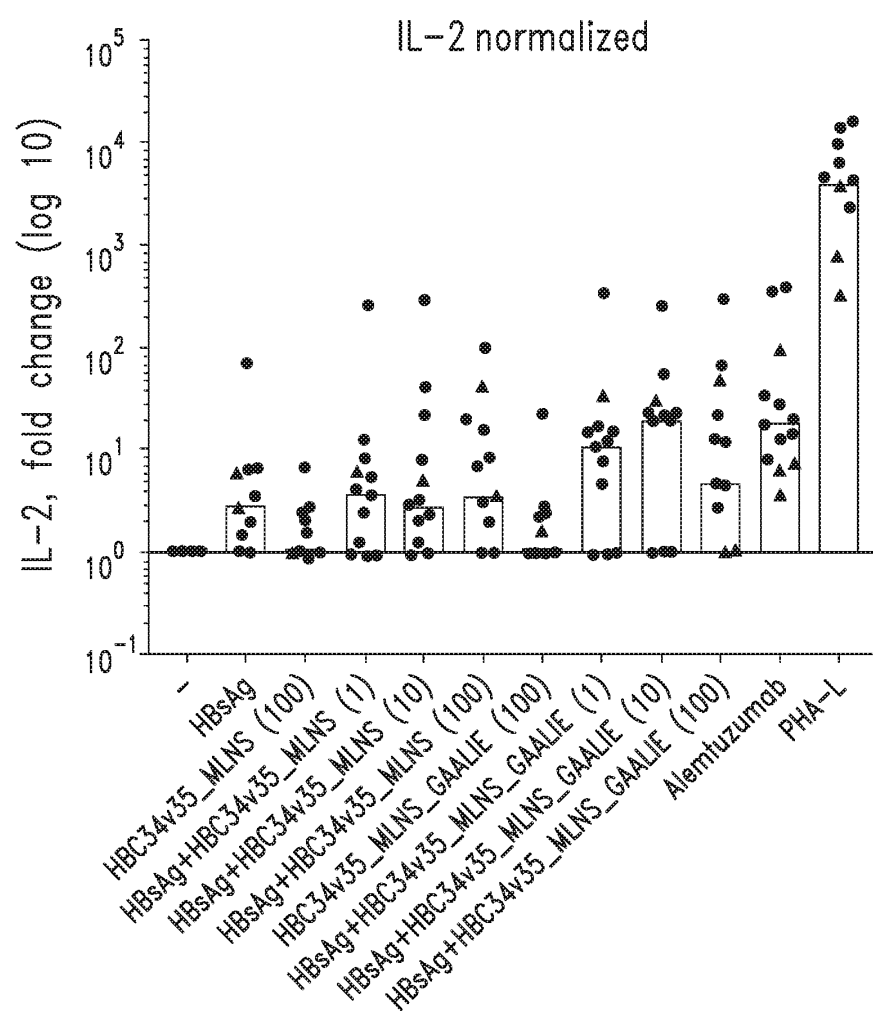


FIG. 23B

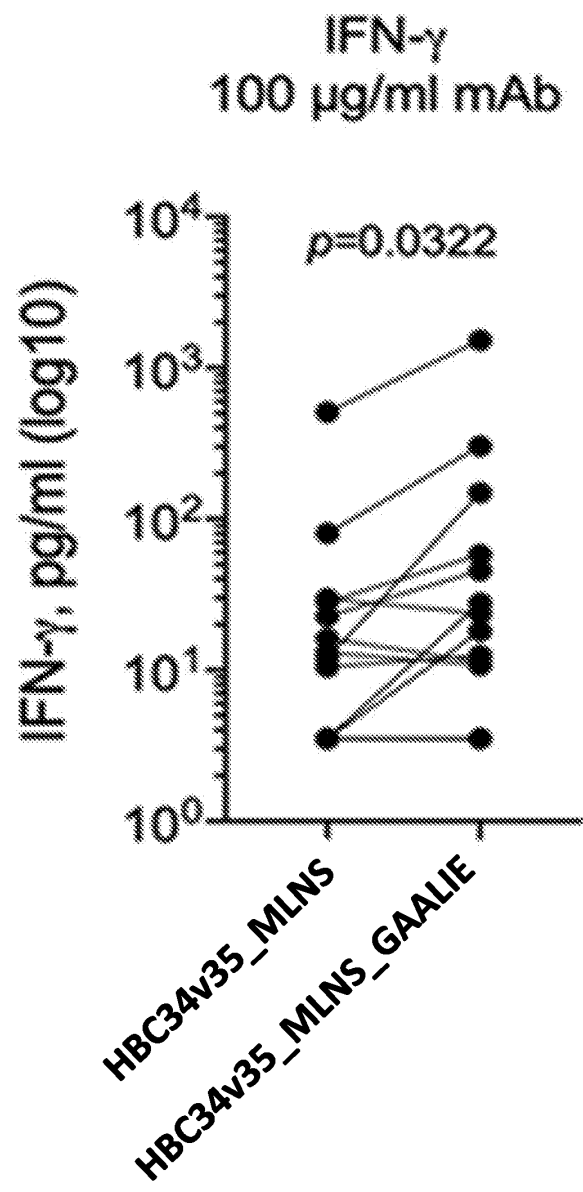


FIG. 24A

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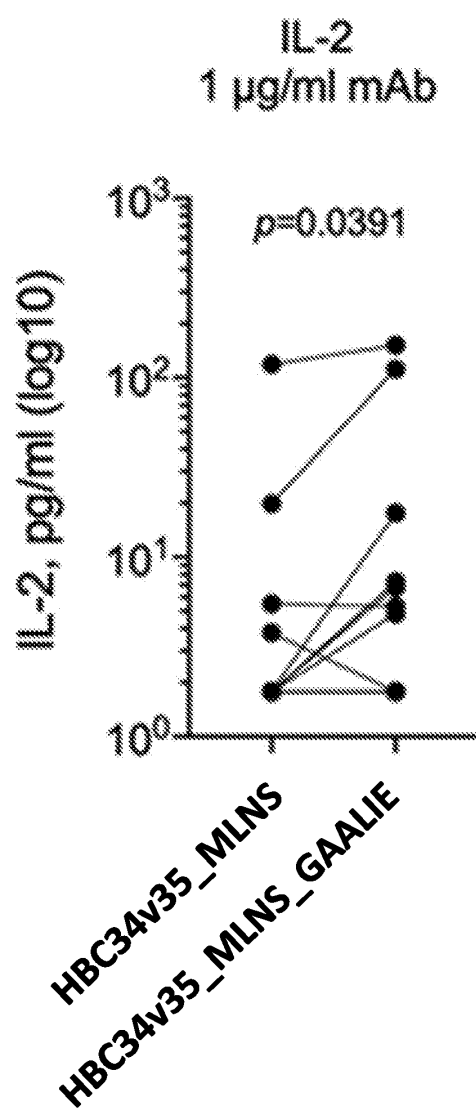


FIG. 24B