

P CrPĩP°C,P°PrPëPS PSP°P»PµP¶PëC,CH PrPs PrCḡCřPiPsPiPs PĩPsPePsP»C-PSPSCİı
P°PSC,PëPiC-CřC,P°PjC-PSPSPëC... PiCḡPµPiP°CḡP°C,C-PI C- C" P°PSC,P°PiPsPSC-CřC,PsPj
PiC-CřC,P°PjC-PSCř C,CḡPëPIP°P»PsC— PrC-C— P· PIPëP±C-CḡPePsPIPsCḡ
PiPµCḡPëC,,PµCḡPëC‡PSPsCḡ P°PSC,P°PiPsPSC-CřC,PëC‡PSPsCḡ P°PeC,PëPIPSC-CřC,Cḡ PrPs
Pķ,-CḡPµC‡PµPĩC,PsCḡC-PI. P"PµCİıPeC- P· PNePsPiPs PjPµC,P°P±PsP»C-C,C-PI
(PrPµP·P»PsCḡP°C,P°PrPëPS C- PNePsPiPs PiC-PrCḡPsPeCřPëP»CHbPsPIP°PSC-
PjPµC,P°P±PsP»C-C,Pë) P·P±PµCḡC-PiP°CḡC,CH P°PSC,PëPiC-CřC,P°PjC-PSPSCř

P°PeC, PēPIPS-ClC, CH C- PjPsP¶CfC, CH C†P°ClC, PePsPIPs C¶PsP±PēC, Pē ClPIC-PMē
PIPSµClPsPe PrPs P·P°PiP°P»CHPSPsC— PµC,, PµPeC, PēPIPSsClC, C- PīC¶PµPīP°C¶P°C, Cr.

P°PsClP»C-PrP¶PµPSPSC¶ C¶CfPīP°C, P°PrPēPSCr *in vitro* Cr PIPēClPsPeC-PMē
PePsPSC†PµPSC, C¶P°C†C-C— PīPsPeP°P·P°P»Pē PiP°P»CHPjCfPIP°PSPSC¶
PrPµPiC¶P°PSCfP»C¶C†C-C— PsPīP°ClPēClC, PēC... PeP»C-C, PēPS, ClPīC¶PēC†PēPSPµPSPµ
C-PjCfPSPsP»PsPiC-C†PSPēPjPē C- PSPµC-PjCfPSPsP»PsPiC-C†PSPēPjPē
PīPsPrC¶P°P·PSPēPeP°PjPē, P° C, P°PePsP¶ PIPēC...C-Pr C†PēC, PsPeC-PSC-PI, P·PsPeC¶PµPjP°
TNF_a, C-P· PsPīP°ClPēClC, PēC... PeP»C-C, PēPS C- PjPsPSPsC†PēC, C-PI P»CHPrPēPSPē.
PµP»C-PSC-C†PSPµ P·PSP°C†PµPSPSC¶ ClPīPsClC, PµC¶PµP¶CfPIP°PSPēC...
PµPeClPīPµC¶PjPµPSC, P°P»CHPSPēC... PrP°PSPēC... C%Pµ C, C-P»CHPePē
PSP°P»PµP¶PēC, CH PiC-PrC, PIPµC¶PrPēC, Pē.

PµC-Pr C†P°Cl PeP»C-PSC-C†PSPēC... PrPsClP»C-PrP¶PµPSC¶ P·P°ClC, PsClCfPIP°PSPSC¶
C¶CfPīP°C, P°PrPēPSCr Cr PrPsP·C- PIC-Pr 2 PjPi PrPs 100 PjPi Cr PrPsP±C¶PsPIPsP»CHC†C-PI
(n=375) C, P° PiP°C†C-C°PSC, C-PI (n=2650) P· P°P»PµC¶PiC-C†PSPēPj C¶PēPSC-C, PsPj C, P°
C...C¶PsPSC-C†PSPsC¶ C-PrC-PsPīP°C, PēC†PSPsC¶ PeC¶PsPīPēPIb¶™ ClPSPePsC¶ PSPµ
P±CfP»Ps PIPēC¶PIP»PµPSPs P·PSP°C†PSPsPiPs PIPīP»PēPICr PīC¶PµPīP°C¶P°C, Cr PSP°
C¶PµP·CfP»CHC, P°C, Pē PµP»PµPeC, C¶PsPeP°C¶PrC-PsPiC¶P°C,, C-C†PSPsPiPs
PrPsClP»C-PrP¶PµPSPSC¶.

P¶C¶PsPSC-C†PSP° C-PrC-PsPīP°C, PēC†PSP° PeC¶PsPīPēPIb¶™ ClPSPeP°
PrPsClP»C-PrP¶CfPIP°P»P°ClC¶ PI CrPjPsPIP°C... PeP»C-PSC-C†PSPsC— PjPsPrPµP»C-
P·P°C...PIPsC¶C¶PIP°PSPSC¶, PsClPeC-P»CHPePē, PSPµP·PIP°P¶P°C¶C†Pē PSP°
PµC, C-PsP»PsPiC-C¶, PīP°C, PsC,, C-P·C-PsP»PsPiC-C¶ P·P°C...PIPsC¶C¶PIP°PSPSC¶
P·P°P»PēC¶P°C°C, CHClC¶ C, P°PePsC¶ P¶, P° C, P°PePsP¶ C, PsPjCr C%Ps PI
PīPµC¶CfPīPµPeC, PēPIC- PīP°C†C-C°PSC, C-PI C-P· C...C¶PsPSC-C†PSPsC¶ C,, PsC¶PjPsC¶
P±CfPrPµ P»PµPiC¶Pµ P·P°P»CrC†PēC, Pē PrPs CrC†P°ClC, C- Cr PrPsClP»C-PrP¶PµPSPSC-.
P¶PµC¶PµP· C, Pµ C%Ps PIPēPIC-P»CHPSPµPSPSC¶ PiC-ClC, P°PjC-PSCr C°
PīC¶PēC†PēPSPSPēPj C,, P°PeC, PsC¶PsPj CrClC-C... PīC¶PsC¶PIC-PI PeC¶PsPīPēPI'ClPSPePē,
PsC†C-PeCrC°C, CHClC¶ PµC,, PµPeC, PēPIPS-ClC, CH C¶CfPīP°C, P°PrPēPSCr PīC¶Pē
PīC¶PsPIPµPrPµPSPSC- ClPēPjPiC, PsPjP°C, PēC†PSPsC— C, PµC¶P°PiC-C—
C...C¶PsPSC-C†PSPsC— C-PrC-PsPīP°C, PēC†PSPsC— PeC¶PsPīPēPI'ClPSPePē C, P° C-PSC¶PēC...
PīC¶PsC¶PIC-PI PeC¶PsPīPēPI'ClPSPePē, ClPe C†Pµ PIPeP°P·P°PSPs Cr PeP»C-PSC-C†PSPēC...
PSP°ClC, P°PSPsPIP°C....

PµC-Pr C†P°Cl PīP»P°C†PµP±Ps-PePsPSC, C¶PsP»CHPsPIP°PSPēC... PrPsClP»C-PrP¶PµPSC¶
C...C¶PsPSC-C†PSPsC— C-PrC-PsPīP°C, PēC†PSPsC— PeC¶PsPīPēPIb¶™ ClPSPePē
C¶CfPīP°C, P°PrPēPS PµC,, PµPeC, PēPIPSs P·PSPēP¶CfPIP°PI ClPµC¶PµPrPSC-PMē P±P°P»
ClPēPjPiC, PsPjC-PI (P·PSPēP¶PµPSPSC¶ PīPsC¶C-PIPSClPSPs C-P· PīPsC†P°C, PePsPIPēPjPē
PīPsPeP°P·PSPēPeP°PjPē: C¶CfPīP°C, P°PrPēPS B b¶" B 57,5 %, B PīP»P°C†PµP±Ps B b¶" B 44,8
) B C, P° B ClPµC¶PµPrPSC¶ B PeC-P»CHPeC-ClC, CH B PIPēClPēPīP°PSC¶ B (54,3 %
B PīPsC¶C-PIPSClPSPs B P·

39,7 %) C†PµC¶PµP· C†PsC, PēC¶Pē C, PēP¶PSC- P»C-PeClPIP°PSPSC¶.

P¶P°C¶PjP°PePsPeC-PSPµC, PēPeP°.

P¶P±ClPsC¶P±C†C-C¶ C- P±C-PsP»PsPiC-C†PSP° PrPsClC, CrPīPSC-ClC, CH.

P CrPīP°C, P°PrPēPS C¶PIPēPrPePs PICrPjPsPeC, CrC°C, CHClC¶ PiC-ClP»C¶
PīPµC¶PsC¶P°P»CHPSPsPiPs PīC¶PēPMēPsPjCr, t_{max} ClC, P°PSPsPIPēC, CH PīC¶PēP±P»PēP·PSPs

B B B B B B B B B B B B B B B B 0,75 PiPsPrPëPSPë PïC-Cl'P»Cll PïcTjPëPNëPsPjCr
C,P°P±P»PµC,PePë. PÿPµCTjPµPrPSCll Pÿ_{max} Cl'C,P°PSPsPIPëP»P° 2,6 PSPi/PjP» PïC-Cl'P»Cll
PsPrPSPsCTjP°P·PsPIPSPiPs PïcTjPëPNëPsPjCr PïPµCTjPsCTjP°P»CHßPSPsC— PrPsP·Pë 10 PjPi C- 4,6
PSPi/PjP» PïC-Cl'P»Cll PsPrPSPsCTjP°P·PsPIPSPiPs PïPµCTjPsCTjP°P»CHßPSPsPiPs
PïcTjPëPNëPsPjCr PrPsP·Pë B B B B B B B B B B B B B B 20 PjPi.
PαP°CtjPjP°PePsPeC-PSPµC,PëPeP° CTjCrPïP°C,P°PrPëPSCr P±CrP»P° P»C-PSC-PNëPSPsCTh
PrP»Cll PrPsP· PIC-Pr 10 PrPs 40 PjPi. PµC-Cl'P»Cll PïcTjPëPNëPsPjCr PrPsP·Pë 10 PjPi PsPrPëPS
CTjP°P· PSP° PrPsP±Cr PïcTjPsC,CllPiPsPj 7 PrPSC-PI Cl'PµCTjPµPrPSCll Pÿ_{max}
Cl'C,P°PSPsPIPëP»P° 3,8 PSPi/PjP». PñPsPSC†PµPSC,CTjP°C†C-Cll PI PïP»P°P·PjC-
P·PSPëP¶CrPIP°P»P°CÍCll P·P° P±C-PµPeCl'PïPsPSPµPSC†C-P°P»CHßPSPsCTh PeCTjPëPIPsCTh P·
Cl'PµCTjPµPrPSC-Pj PïPµCTjC-PsPrPsPj PSP°PïC-PIIPëPIPµPrPµPSPSCll 5,9 PiPsPrPëPSPë.
PñPsPµC,,C-C†C-C"PSC, P·PI'CllP·CrPIP°PSPSCll CTjCrPïP°C,P°PrPëPSCr P· P±C-P»PeP°PjPë
PïP»P°P·PjPë Cl'C,P°PSPsPIPëPI 98,5BTh"99 %.

PhCfPSP±P»PëPIC- PiCfCfPiPë PiP°C+C-C"PSC,C-PI

PJ C...PsPrC- PrPsCfP»C-PrP¶PµPSPSC¶ P·P° CrC±P°CfC,Ch P·PrPsCfPSPiPëC...
PrPsP±CfPSPiPSP»ChC†C-PI PrP»C¶ PiPsCfC-PIPSC¶PSPSC¶ C¶PµP·CfP»ChC,P°C,C-PI,
PsC,C¶PëPjP°PSPëC... Cr PjPsP»PsPrPëC... PrPsCfPSPiP»PëC... PsCfC-P± C,P° PsCfC-P±
P»C-C,PSCHbPsPiPs PIC-PeCr, PiPµP»PëC±PëPSPë AUC C- PŸ_{max} C¶CfPiP°C,P°PrPëPSCr
P±CfP»Pë PiPëC%PëPjPë Cr PsCfC-P± P»C-C,PSCHbPsPiPs PIC-PeCr Cr
PiPsCfC-PIPSC¶PSPSC- P· PrP°PSPëPjPë, PsC,C¶PëPjP°PSPëPjPë Cr PjPsP»PsPrPëC...
PrPsCfPSPiP»PëC... PsCfC-P±. PTM PjPsPIC-C¶PSPs, C†Pµ PsP±CfPjPsPiP»PµPSPs
P·PSPëP¶PµPSPSC¶Pj PiPµC†C-PSPePsPiPsPjPµC,P°P±PsP»C-P·PjCr PiC¶Pë PiPµC¶C¶PsPjCr
PiC¶PSPC...PsPrP¶PµPSPSC- C†PµC¶PµP· PiPµC†C-PSPeCr Cr PsCfC-P± P»C-C,PSCHbPsPiPs
PIC-PeCr. P©PsPrPs B PjPµC,P°P±PsP»C-C,C-PI PIC-PrPjC-PSPSPsCfC,PµPNë PjC-P¶
PiPsPeP°P·PSPëPeP°PjPë AUC C- PŸ_{max} Cr PjPsP»PsPrPëC... PrPsCfPSPiP»PëC... PsCfC-P± C,P°
PsCfC-P± P»C-C,PSCHbPsPiPs PIC-PeCr PSPµ C¶PiPsCfC,PµC¶C-PiP°P»PsCfC¶.
PŸPµC¶PµPrPSC-PNë PiPµC¶C-PsPr PSP°PiC-PIPiPëPiPµPrPµPSPSC¶ C¶CfPiP°C,P°PrPëPSCr Cr
P»C-C,PSC-C... C- Cr PjPsP»PsPrPëC... PrPsP±CfPSPiPSP»ChC†C-PI CfC,P°PSPsPiPëPI 8,7
PiPsPrPëPSPë C- 5,9 PiPsPrPëPSPë PIC-PrPiPsPIC-PrPSPs. PhCfPeC-P»ChPePë
C¶PµP·CfP»ChC,P°C,Pë PrP»C¶ C¶CfPiP°C,P°PrPëPSCr C- PrP»C¶ PNëPsPiPs
PjPµC,P°P±PsP»C-C,C-PI PSPµ P±CfP»Pë PeP»C-PSC-C†PSPs P·PSP°C±CfC%PëPjPë, P±CfPI
P·C¶PSP±P»PµPSPëPNë PiPëCfPSPsPiPsPe, C%Ps PiC¶Pë PiC¶PëP·PSP°C†PµPSPSC- 10 PjPi
P»C-PeP°C¶CfChPePsPiPs P·P°CfPSP±Cf PiP°C+C-C"PSC,P°Pj P»C-C,PSCHbPsPiPs PIC-PeCr
PePsC¶PµPeC†C-C¶ PrPsP·Pë PSPµ PiPsC,C¶C-P±PSP°.

P"PsPeP»C-PSC-C†PSC- PrP°PSC- P· P±PµP·PiPµPePë

P"°PSC- PrPsPeP»C-PSC-C†PSPëC... PrPsCfP»C-PrP¶PµPSCHb PSPµ PiPeP°P·CfChC,Ch PSP°
C-CfPSCrPiP°PSPSC¶ PsCfPSP±P»PëPiPsPiPs C¶PëP·PëPeCr PrP»C¶ P»ChPrCfChPePsPiPs
PsC¶PiP°PSC-P·PjCr PSP° PiC-PrCfC,P°PIC- CfC,P°PSPrP°C¶C,PSPëC...
PrPsCfP»C-PrP¶PµPSCHb C,,P°C¶PjP°PePsP»PsPiC-C†PSPsC— C,PsPeCfPëC†PSPsCfC,C- PiC¶Pë
PiPsPIC,PsC¶PSPsPjCr P·P°CfC,PsCfCfPiP°PSPSC-, PiPµPSPsC,PsPeCfPëC†PSPsCfC,C- C,P°
PeP°PSC†PµC¶PSPiPµPSPSPsCfC,C-.

P"PsP·Pë C¶CfPiP°C,P°PrPëPSCr, C%Ps Cr 100 C¶P°P·C-PI PiPµC¶PµPiPëC%CrPiP°P»Pë
C¶PµPePsPjPµPSPrPsPiP°PSCr PeP»C-PSC-C†PSCr PrPsP·Cr (10 PjPi), PSPµ PiPiP»PëPiP°P»Pë
PSP° C-PSC,PµC¶PiP°P»Pë QTc C,P° QRS C- PSPµ C¶PiC¶PëC†PëPSC¶P»Pë C¶PëPjPiC,PsPjC-PI
P°C¶PëC,PjC-C— Cr C¶C-P·PSPëC... PiPëPrC-PI C,PiP°C¶PëPS, PSP°PiC¶PëPeP»P°Pr Cr
C%CrC¶C-PI, PjPsC¶CfChPePëC... C¶PiPëPSPsPe C,P° C¶PsP±P°Pe. P CrPiP°C,P°PrPëPS C,P°
PNëPsPiPs PsCfPSPsPiPSPëPNë PjPµC,P°P±PsP»C-C, PI PsC¶PiP°PSC-P·PjC- P»ChPrPëPSPë, 3-
PiC-PrC¶PSPeCfPëPrPµP·P»PsC¶P°C,P°PrPëPS, PSPµ PiPiP»PëPiP°ChC,Ch PSP°
PiPsC,PµPSC†C-P°P» PrC-C— C¶PµC¶C†PµPiPsPj'CiP·Cr Cr PiPsP»PsPePSP°C...
PµCrC¶PeC-PSCHb" C¶PsP±P°Pe Cr PePsPSC†PµPSC,C¶P°C†C-C¶C..., C%Ps PjC-PSC-PjCrPj Cr
2000 C¶P°P·C-PI PiPëC%C- P·P° PjP°PeCfPëPjP°P»ChbPSCr PePsPSC†PµPSC,C¶P°C†C-Ch PI
PiP»P°P·PjC- P»ChPrPëPSPë PiC¶Pë P·P°CfC,PsCfCfPiP°PSPSC- 10 PjPi PiC¶PµPiP°C¶P°C,Cr.
PµC-Pr C†P°Cf PrPsCfP»C-PrP¶PµPSPSC¶ PiPiP»PëPiCr C¶CfPiP°C,P°PrPëPSCr PSP°
PeP»PsPSPsPiP°PSPëPNë PiPµPS C¶PiPµC†PëC,,C-C†PSPsPiPs PeP°P»C-C"PiPsPiPs PeP°PSP°P»Cr
C¶PµC¶C†C¶ PIC-PS PiC¶PëPiPSC-C†CfPiP°PI C†PµPNë PeP°PSP°P» Cr
PePsPSC†PµPSC,C¶P°C†C-C—, C%Ps P±CfP»P° Cr 1685 C¶P°P·C-PI PiPëC%PsCh P·P°
PjP°PeCfPëPjP°P»ChbPSCr PePsPSC†PµPSC,C¶P°C†C-Ch PI PiP»P°P·PjC-, CiPeP°
PrPsCfC¶PiP°P»P°CfC¶ PiC¶Pë P·P°CfC,PsCfCfPiP°PSPSC- 10 PjPi PiC¶PµPiP°C¶P°C,Cr.
P"µP·P»PsC¶P°C,P°PrPëPS, PjPµC,P°P±PsP»C-C, C-P· PSP°PNëPiPëC%PsCh
P°PeC,PëPiPSC-CfC,Ch, PSPµ C†PëPSPëC,Ch P¶PsPrPSPsPiPs PiPiP»PëPiCr PiC¶Pë

PePsPSC†PμPSC, C₇H^oC†C-C— 10 PjPeP₇PsP»CH/P». B P^oPsC₇P»C-PrP¶PμPSPSC¶
C₇PsP·PīPsPrC-P»C₇ PI C, PeP^oPSPëPSP^oC... C%_oC₇C-PI C₇P^oPrC-PsP^oPeC, PëPIPSPs
PjC-C†PμPSPsPiPs C₇C₇PīP^oC, P^oPrPëPSC₇ PīPsPeP^oP·P^oP»Pë, C%_oPs PIC-PS PSPμ
PSP^oPePsPīPëC†C₇C, CHC₇C¶ PI C, PeP^oPSPëPSP^oC... C₇PμC₇C†C¶.

PŸPīPsC₇C, PμC₇C-PiP^oP»PsC₇C¶ P·PSP^oC†PSPμ P·PSPëP¶PμPSPSC¶
C,, PμC₇C, PëP»CHPSPsC₇C, C- C¶Pe C₇P^oPjC†C-PI, C, P^oPe C- C₇P^oPjPsPe C%_oC₇C-PI PīC₇Pë
P·P^oC₇C, PsC₇C₇PiP^oPSPSC-B PrPsP·Pë 120 PjPi/PePi/PrPsP±C₇, PePsP»Pë
PjP^oPeC₇PëPjP^oP»CHPSP^o PePsPSC†PμPSC, C₇H^oC†C-C¶ C₇ 268 C₇P^oP·C-PI PIPëC%_oP^o P·P^o C_{max}
PI PsC₇PiP^oPSC-P·PjC- P»CHPrPëPSPë, C¶PeP^o PrPsC₇C¶PiP^oC, CHC₇C¶ PīC₇Pë
P·P^oC₇C, PsC₇C₇PiP^oPSPSC- C, PμC₇P^oPiPμPIC, PëC†PSPsC— PrPsP·Pë (10 PjPi/PrPsP±C₇).
PμPsPIC-PrPsPjP»C¶P»PsC₇C¶ PīC₇Ps C, PsPeC₇PëC†PSPëPN₂ PIPiP»PëPI PSP^o PīP»C-Pr
(P·P^oC, C₇PëPjPeP^o C₇PsP·PIPëC, PeC₇, PSPμPīPsPIPSPμ C₇C, PIPsC₇PμPSPSC¶
PeC-C₇C, PePsPIPSC— C₇PμC†PsPIPëPSPë, PSPμP·PSP^oC†PSC- PIC-PrC...PëP»PμPSPSC¶
C₇PsP·PIPëC, PeC₇ C₇PePμP»PμC, P^o) C₇ C%_oC₇C-PI PīC₇Pë C, PsPeC₇PëC†PSPëC... PrP»C¶
C₇P^oPjPsPe PrPsP·P^oC... (25 C, P^o 120 PjPi/PePi/PrPsP±C₇). PμC-Pr C†P^oC₇
PrPsC₇P»C-PrP¶PμPSC₇ PSP^o PeC₇PsP»C¶C... C, PsPeC₇PëC†PSPëPN₂ PIPiP»PëPI PSP^o
C₇PsP·PIPëC, PsPe C₇PīPsC₇C, PμC₇C-PiP^oPiC₇C¶ PīC₇Pë P·P^oC₇C, PsC₇C₇PiP^oPSPSC- PrPsP·
PrPs 100 PjPi/PePi. P C-PIPμPSC₇, C%_oPs PSPμ PIPëPeP»PëPeP^oC C€PeC-PrP»PëPIPsC—
PrC-C—, PrP»C¶ C%_oC₇C-PI C₇C, P^oPSPsPIPëC, CH 5 PjPi/PePi/PrPsP±C₇, P^o PrP»C¶
PeC₇PsP»C-PI B₇ 100 PjPi/PePi/PrPsP±C₇, PīC₇Pë C†CHPsPjC₇ C_{max} PIC-PrPīPsPIC-PrPSPs C₇ 45
C, P^o 116 C₇P^oP·C-PI PIPëC%_oP^o P·P^o PePsPSC†PμPSC, C₇H^oC†C-C₇, C%_oPs
PrPsC₇C¶PiP^oC, CHC₇C¶ PīC₇Pë P·P^oC₇C, PsC₇C₇PiP^oPSPSC- C, PμC₇P^oPiPμPIC, PëC†PSPsC—
PrPsP·Pë, C₇ P»CHPrPëPSPë (10 PjPi/PrPsP±C₇).

РљР»С-РSC-С†РSC- С...Р°С₇Р°РєС, РμС₇РєС₇С, РєРєРє.

PμPsPeP^oP·P^oPSPSC¶.

PŸPëPjPiC, PsPjP^oC, PëC†PSPμ P»C-PeC₇PiP^oPSPSC¶ P^oP»PμC₇PiC-C†PSPsPiPs C₇PëPSC-C, C₇ C-
PeC₇PsPīPëPiB₇™ C¶PSPePë C₇ PrPsC₇PsC₇P»PëC... C, P^o PīC-PrP»C-C, PeC-PI PIC-PePsPj PIC-Pr
B B B B B B B B B B B B B B 12 C₇PsPeC-PI.

PμC₇PsC, PëPīPsPeP^oP·P^oPSPSC¶.

P^oC-PiPμC₇C†C₇C, P»PëPIC-C₇C, CH PrPs PrC-CHC†PsC— C₇PμC†PsPIPëPSPë P^oP±Ps PrPs
P±C₇PrCH-C¶PePsPiPs C-PSC€PsPiPs PePsPjPīPsPSPμPSC, P^o PīC₇PμPīP^oC₇P^oC, C₇.

***P·P·P^oC^oPjPsPrC-C¶ P· C-PSC€PëPjPë P»C-PeP^oC₇C₇CHPePëPjPë P·P^oC₇PsP±P^oPjPë C, P^o
C-PSC€C- PIPëPrPë PIP·P^oC^oPjPsPrC-PN₂.***

P·P·P^oC^oPjPsPrC-C¶ C, P^oP±P»PμC, PsPe C₇C₇PīP^oC, P^oPrPëPSC₇ PīPs 10 PjPi C-P·
C-PSC€PëPjPë P»C-PeP^oC₇C₇CHPePëPjPë P·P^oC₇PsP±P^oPjPë
PrPsC₇P»C-PrP¶C₇PiP^oP»P^oC₇CH C₇ PrPsC₇PsC₇P»PëC... C, P^o PrC-C, PμPN₂ PIC-PePsPj
PIC-Pr 12 C₇PsPeC-PI.

P'PīP»PēPI C-PSC€PēC... P»C-PeP°CḡCÍCHPePēC... P·P°CÍPsP±C-PI PSP° PrC-CH
CḡCḡPīP°C,P°PrPēPSCḡ

PŸP»C-Pr CrPSPēPeP°C,Pē CÍCrPīCrC,PSCHPsPiPs P·P°CÍC,PsCÍCrPIP°PSPSCİ
PīPsC,CrP¶PSPēC... C-PSPiC-P±C-C,PsCḡC-PI CYP3A4 (PSP°PīCḡPēPeP»P°Pr
C-C,CḡP°PePsPSP°P·PsP»Cr, PePμC,PsPePsPSP°P·PsP»Cr, PIPsCḡPēPePsPSP°P·PsP»Cr,
PīPsP·P°PePsPSP°P·PsP»Cr, C-PSPiC-P±C-C,PsCḡC-PI P'P†P> PīCḡPsC,PμP°P·Pē,
PeP»P°CḡPēC,CḡPsPjC-C†PēPSCr, PSPμC,,P°P·PsPrPsPSCr), P° PīPsPjC-CḡPSC-
C-PSPiC-P±C-C,PsCḡPē CYP3A4 (PμCḡPēC,CḡPsPjC-C†PēPS, C,,P»CrPePsPSP°P·PsP»,
PrPēP»C,C-P°P·PμPj) PīPsC,CḡC-P±PSPs P·P°CÍC,PsCÍPsPICrPIP°C,Pē P·
PsCÍPsP±P»PēPIPsCH PsP±PμCḡPμP¶PSC-CÍC,CH.

PŸCrPjC-CÍPSPμ PīCḡPēP·PSP°C‡PμPSPSCİ CḡCrPīP°C,P°PrPēPSCr Cr PrPsP·C- 20 PjPi
C- PePμC,PsPePsPSP°P·PsP»Cr P°P±Ps PμCḡPēC,CḡPsPjC-C†PēPSCr PīC-PrCÍPēP»CHC"
CÍPēCÍC,PμPjPSCr PrC-CH CḡCrPīP°C,P°PrPēPSCr PI 10 CḡP°P·C-PI C- PI 2Bḡ"3
CḡP°P·Pē PIC-PrPīPsPIC-PrPSPs. P|C- PjPsPrPēC,,C-PeP°C†C-C— PSPμ
CÍCrPīCḡPsPIPsrP¶CÍCHC,CHCÍCİ P·PjC-PSP°PjPē C-PSC,PμCḡPIP°P»Cr QT P°P±Ps
P·P±C-P»CHC€PμPSPSCİPj PīPsP±C-C‡PSPēC... CḡPμP°PeC†C-PNē
PīPsCḡC-PIPSCİPSPs P· PsPeCḡPμPjPēPj P·P°CÍC,PsCÍCrPIP°PSPSCİPj
PIPeP°P·P°PSPēC... PīCḡPμPīP°CḡP°C,C-PI.

P'P·P°C"PjPsPrC-Cİ P· PiCḡPμPNēPīC,,CḡCḡC,PsPj

PhPrPSPsC‡P°CÍPSPēPNē PīCḡPēPNēPsPj PiCḡPμPNēPīC,,CḡCrC,PsPIPsPiPs CÍPsPeCr PI
3,5 CḡP°P·P° PīC-PrCÍPēP»CHC" P·P°PīP°P»CHPSCr PrC-CH CḡCrPīP°C,P°PrPēPSCr.
PḡPμ CÍP»C-Pr PIP¶PēPIP°C,Pē PiCḡPμPNēPīC,,CḡCrC,PsPIPēPNē CÍC-Pe
PsPrPSPsC‡P°CÍPSPs P· PīCḡPēPNēPsPjPsPj PīCḡPμPīP°CḡP°C,Cr.

P'PīP»PēPI CḡCḡPīP°C,P°PrPēPSCḡ PSP° C-PSC€C- P»C-PeP°CḡCÍCHPeC- P·P°CÍPsP±Pē

PŸP»C-Pr P· PsP±PμCḡPμP¶PSC-CÍC,CH P·P°CÍC,PsCÍPsPICrPIP°C,Pē
CḡCrPīP°C,P°PrPēPS C-P· C-PSC€PēPjPē PīCḡPμPīP°CḡP°C,P°PjPē P· PICrP·CHPePēPj
C,PμCḡP°PīPμPIC,PēC‡PSPēPj PrC-P°PīP°P·PsPSPsPj, PsCÍPeC-P»CHPePē
C-PSC,,PsCḡPjP°C†C-Cİ PīCḡPs PNēPsPiPs PIPīP»PēPI PSP° C†C- PīCḡPμPīP°CḡP°C,Pē
PsP±PjPμP¶PμPSP°.

P'P·P°C"PjPsPrC-Cİ P· P°P»PePsPiPsP»PμPj

PμC-CÍP»Cİ PīCḡPēPNēPsPjCr P°P»PePsPiPsP»CH PrPsP·P° CḡCrPīP°C,P°PrPēPSCr 10 PjPi
PIPēCİPIP»CİC" PSPμP·PSP°C‡PSPēPNē PIPīP»PēPI PSP° CḡPμP·CrP»CHC,P°C,Pē
PrPμCİPePēC... C,PμCÍC,C-PI PSP° PīCÍPēC...PsPjPsC,PsCḡPSCr P°PeC,PēPIPSC-CÍC,CH, C%oPs
P·PSP°C‡PSPs PSPμ PIC-PrCḡC-P·PSCİC"C,CHCÍCİ PIC-Pr PIPīP»PēPICr PīCḡPēPNēPsPjCr
C,C-P»CHPePē PsPrPSPsPiPs P°P»PePsPiPsP»CH. P"PsP·P° 20 PjPi PīC-PrCÍPēP»CHPIP°P»P°
P·PjC-PSPē, CÍPīCḡPēC‡PēPSPμPSC- PīCḡPēPNēPsPjPsPj P°P»PePsPiPsP»CH.

P'P·P°C"PjPsPrC-Cİ P· PrPμPīCḡPμCÍP°PSC,P°PjPē P|PḡPŸ

PīPe C- Cr CḡP°P·C- P·P°CÍC,PsCÍCrPIP°PSPSCİ C-PSC€PēC...
P°PSC,PēPiC-CÍC,P°PjC-PSPSPēC... PīCḡPμPīP°CḡP°C,C-PI, PSPμ PjPsP¶PSP°

PIPëPeP»CĤC±PëC,Pë PIP·P°C”PjPsPrC-C— P· PrPμPïCĤPμCÍP°PSC,P°PjPë P|PǵPŸ.

P'P·P°C”PjPsPrC-CĬ P·C- CÍC,P°C,PëPSP°PjPë

P'PμP·CÍPëPjPïC,PsPjPSPμ PïC-PrPIPëC%PμPSPSCĬ
PeCĤPμP°C,PëPSC,,PsCÍC,,PsPeC-PSP°P·Pë C-PSPsPrC- PIC-PrPjC-C±P°P»Pë PïC-Pr
C±P°CÍ PeP»C-PSC-C±PSPëC... PrPsCÍP»C-PrP¶PμPSCĤ CĤCÍPïP°C,P°PrPëPSCÍ.
P PëP·PëPe PïCĤPë PIP·P°C”PjPsPrC-C— P·C- CÍC,P°C,PëPSP°PjPë, PrPμCĬPeC- P·
PSPëC... C,P°PePsP¶ PjPμC,P°P±PsP»C-P·CÍCĤC,CHCÍCĬ C-P·PsC,,PμCĤPjPμPSC,PsPj
CYP3A4 C†PëC,PsC...CĤPsPjCÍ P450, PSPμPIC-PrPsPjPëPN. PŸPsPjCÍ
CĤCÍPïP°C,P°PrPëPS CÍP»C-Pr P· PsP±PμCĤPμP¶PSC-CÍC,CĤ
P·P°CÍC,PsCÍPsPICÍPIP°C,Pë PïCĤPë PsPrPSPsC±P°CÍPSPsPjCÍ
PïCĤPëP·PSP°C±PμPSPSC- P·C- CÍC,P°C,PëPSP°PjPë.

P'P·P°C”PjPsPrC-CĬ P· PjC-PrP°P·PsP»P°PjPsPj

PμC-CÍP»CĬ PïCĤPëPNPsPjCÍ PrPsP·Pë CĤCÍPïP°C,P°PrPëPSCÍ 10 PjPi CÍ
PePsPjP±C-PSP°C†C-C— P· 7,5 PjPi PjC-PrP°P·PsP»P°PjPsPj, PïC-PrPIPëC%PμPSPSCĬ
PμPeCÍPïPsP·PëC†C-C— (Cmax C,P° AUC) PjC-PrP°P·PsP»P°PjCÍ P±CÍP»P° PrPμC%Ps
PIPëC%PsCĤ. P— C†C-C”C— PïCĤPëC±PëPSPë CĤCÍPïP°C,P°PrPëPS PrC-C” CĬPe
P»PμPïPePëPN C-PSPiC-P±C-C,PsCĤ

CYP3A4.

PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍC¿PIP°PSPSCĬ.

PǵPμ CĤPμPePsPjPμPSPrCÍC”C,CHCÍCĬ PsPrPSPsC±P°CÍPSPëPN PïCĤPëPNPsPj
CĤCÍPïP°C,P°PrPëPSCÍ P· PïCĤPμPNPïC,,CĤCÍC,PsPIPëPj CÍPsPePsPj (PrPëPI. CĤPsP·PrC-P»
B«P'P·P°C”PjPsPrC-CĬ P· C-PSC€PëPjPë P»C-PeP°CĤCÍCHPePëPjPë P·P°CÍPsP±P°PjPë C,P°
C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PN»B»).

PŸP»C-Pr CÍPSPëPeP°C,Pë PsPrPSPsC±P°CÍPSPsPiPs P·P°CÍC,PsCÍCÍPIP°PSPSCĬ
CĤCÍPïP°C,P°PrPëPSCÍ C-P· PïPsC,CÍP¶PSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë CYP3A4, P° P·
PïPsPjC-CĤPSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë CYP3A4 BĤ“ P·P°CÍC,PsCÍPsPICÍPIP°C,Pë C-P·
PsCÍPsP±P»PëPIPsCĤ PsP±PμCĤPμP¶PSC-CÍC,CĤ (PrPëPI. CĤPsP·PrC-P»
B«P'P·P°C”PjPsPrC-CĬ P· C-PSC€PëPjPë P»C-PeP°CĤCÍCHPePëPjPë P·P°CÍPsP±P°PjPë C,P°
C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PN»B»).

PĤPsP¶Pμ PIPëPSPëPePSCÍC,Pë PSPμPsP±C...C-PrPSC-CÍC,CH CÍ PePsCĤPμPeC†C-C— PrPsP·Pë
C±CÍC,P»PëPIPëC... CÍCÍP±CÍC,CĤP°C,C-PI PrP»CĬ CYP3A4 (PSP°PïCĤPëPeP»P°Pr
CÍPëPjPIP°CÍC,P°C,PëPSCÍ, P»PsPIP°CÍC,P°C,PëPSCÍ) C,P° CÍCÍP±CÍC,CĤP°C,C-PI
C,,PμCĤPjPμPSC,CÍ CYP3A4 C-P· PICÍP·CHPePëPj C,PμCĤP°PïPμPIC,PëC±PSPëPj
PrC-P°PïP°P·PsPSPsPj (PSP°PïCĤPëPeP»P°Pr C†PëPeP»PsCÍPïPsCĤPëPSCÍ,
C,P°PeCĤPsP»C-PjCÍCÍCÍ, CÍPëCĤPsP»C-PjCÍCÍCÍ, PμPIPμCĤPsP»C-PjCÍCÍCÍ,
C†PëP·P°PïCĤPëPrCÍ), PsCÍPeC-P»CHPePë CĤCÍPïP°C,P°PrPëPS PjPsP¶Pμ
PïC-PrPIPëC%CÍPIP°C,Pë C—C...PSC- PïP»P°P·PjPsPIC- PePsPSC†PμPSC,CĤP°C†C-C— (PrPëPI.
CĤPsP·PrC-P» B«P'P·P°C”PjPsPrC-CĬ P· C-PSC€PëPjPë P»C-PeP°CĤCÍCHPePëPjPë
P·P°CÍPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PN»B»).

РљР°СђРrС-РsР»РsРiС-СђРSP° Р±РµР·РiРµРµР° СђСrРiР°С,Р°РrРёРSCr РIРёРIСђР°Р»Р°СђСђ РiС-Рr СђР°Сђ РrРsСђР»С-РrР¶РµРSPSC¶ Thorough QT/QTc. Р—Р°СђС,РsСђСrРIР°РSPSC¶ РrРsР· СђСrРiР°С,Р°РrРёРSCr, С°Рs Сr 10 СђР°Р·С-РI РIРёС°С- Р·Р° С,РµСђР°РiРµРIС,РёСђРSC-, РSPµ РIРёС¶РIР»С¶Р»Рs Р¶РsРrРSPsРiРs РIРiР»РёРIСr РSP° СђРµР·СrР»СђС,Р°С,Рё Р·РљР°-РrРsСђР»С-РrР¶РµРPSCH, С,РsРjСr РNёРsРiРs Р·Р°СђС,РsСђСrРIР°РSPSC¶ РSPµ РIРёРёР»РёРёР°С" РiРёС,Р°РSCH Р· РёР°СђРrС-РsР»РsРiС-СђРSPsС— Р±РµР·РiРµРµРё. РђРrРSP°Рё СђСrРiР°С,Р°РrРёРPS СђР»С-Рr РiСђРёР·РSP°СђР°С,Рё Р· РsР±РµСђРµР¶РµР¶РSC-СђС,Сђ РiР°СrС-С"РSC,Р°Рj Р· РiРsРrРsРIР¶РµРSPёРj С-РSC,РµСђРIР°Р»Р»РsРj QT, РiР°СrС-С"РSC,Р°Рj Р· РSPµСђРёРsСђРёРiРsРIР°РSPsСђ РiС-РiРsРёР°Р»С-С"РjС-С"Сђ, РiР°СrС-С"РSC,Р°Рj Р·С- СђС,С-РNёРёРёРjРё РiСђРsР°СђРёС,РjС-СђРSPёРjРё СђС,Р°РSP°РjРё, С,Р°РёРёРjРё С¶Рё РёР»С-РSC-СђРSPs Р·РSP°СrС°Р° Р±СђР°РrРёРёР°СђРrС-С¶, РiРsСђС,СђР° С-СёРµРjС-С¶ РjС-РsРёР°СђРr°.

Р СrРiР°С,Р°РrРёРPS Сr С,Р°Р±Р»РµС,РёР°С... РiРs 10 РjРi РSPµРsР±С...С-РrРSPs Р· РsР±РµСђРµР¶РµР¶РSC-СђС,Сђ РiСђРёР·РSP°СђР°С,Рё Р»С-С,РSC-Рj РiР°СrС-С"РSC,Р°Рj (РIС-РёРsРj РIС-Рr 65 СђРsРёС-РI).В РrРsСђР° РI С...РsРrС- РёР»С-РSC-СђРSPёС... РIРёРiСђРsР±СrРIР°РSCH РSPµ РIС-РrРjС-СђР°Р»Рё Р·Р°РiР°Р»С»СђРSPёС... РIС-РrРjС-РSPSPСђС,РµРNё РI РµС,,РµРёС,РёРIРSPsСђС,С- Р°Р±Рs Р±РµР·РiРµРµРiСr, РSPµ РjРsР¶РSP° РIРёРёР»С»СђСђРёС,Рё РjРsР¶Р»РёРiРsСђС,С- РiС-РrРIРёС°РµРSPsС— СђСrС,Р»РёРiРsСђС,С- Сr РrРµС¶РёС... РiР°СrС-С"РSC,С-РI Р»С-С,РSCHРsРiРs РIС-РёСr, РsСђРёС-Р»СђРёРё РёС-Р»СђРёС-СђС,Сђ РiР°СrС-С"РSC,С-РI, С¶РёС- Р±СђР°Р»Р»Рё РiСrСђР°СђС,Сђ Сr РIРёРiСђРsР±СrРIР°РSPSC¶C..., Р±СrР»Р° РSPµР·РSP°СђРSPsСђ (РrРёРI. СђРsР·РrС-Р» В«Р°Р°СђРjР°РёРsР»РsРiС-СђРSC- РIР»Р°СђС,РёРiРsСђС,С-В»).

РµСђРs РiСђРёР·РSP°СђРµРSPSC¶ РrС-С,С¶Рj РIС-РёРsРj РiРsРSP°Рr 12 СђРsРёС-РI С- РiР°СrС-С"РSC,Р°Рj Р· РSPёСђРёРsРIРёРjРё Р°Р±Рs РiРµСђС-РSPёРsРIРёРjРё РiРsСђСrСёРµРSPSC¶РjРё РrРёРI. Сr СђРsР·РrС-Р»С- В«РiРiРsСђС-Р± Р·Р°СђС,РsСђСrРIР°РSPSC¶ С,Р° РrРsР·РёВ».

РђСђРёС-Р»СђРёРё С,Р°Р±Р»РµС,РёРё СђСrРiР°С,Р°РrРёРSCr РjС-СђС,С¶С,Сђ Р»Р°РёС,РsР·Сr, РiСђРµРiР°СђР°С, РSPµ СђР»С-Рr РiСђРёРNёРjР°С,Рё РiР°СrС-С"РSC,Р°Рj Р· СђС-РrРёРjРё СђРiР°РrРёРsРIРёРjРё РiСђРsР±Р»РµРjРё РiР°Р»Р»Р°Р»Рё РiР°Р»Р»Р°Р»Р·РSPsС— РSPµРiРµСђРµРSPsСђРёРjРsСђС,С-, РrРµС,,С-СrРёС,Сr Р»Р°РёС,Р°Р·Рё Р»Р°РiРiР° Р°Р±Рs РiР»С»СђРёРsР·Рs-РiР°Р»Р»Р°Р»Р·РSPsС— РjР°Р»С»Р°СђРsСђР±СrС-С—.

Р—Р°СђС,РsСђСrРIР°РSPSC¶ Сё РiРµСђР-РsРr РIР°РiС-С,РSPsСђС,С- Р°Р±Рs РiРsРrСёРIР°РSPSC¶ РiСђСёРrРrСђ.

Р'Р°РiС-С,РSC-СђС,Сђ

РrСђРSCrСђС,Сђ РsР±РjРµР¶РµРSC- РrР°РSC- С°РsРrРs Р·Р°СђС,РsСђСrРIР°РSPSC¶ СђСrРiР°С,Р°РrРёРSCr РIР°РiС-С,РSPёРjРё Р¶IС-РSPёРj. Р"РsСђР»С-РrР¶РµРSPSC¶ РSP° С,РIР°СђРSP°С... РSPµ СђРIС-РrСђР°С,Сђ РiСђРs Р±РµР·РiРµРiСђРµСђРrРSC-РNё Р°Р±Рs РsРiРsСђРµСђРµРsРIР°РSPёРNё СёРёС-РrР»РёРiРёРNё РIРiР»РёРI РSP° РµРjР±СђС-РsРS/РiР»С-Рr, РiРµСђРё- С,Р° РiРsСђС,РSP°С,Р°Р»С»СђРSPёРNё СђРsР·РiРёС,РsРё (РrРёРI. СђРsР·РrС-Р» В«Р°Р°СђРjР°РёРsР»РsРiС-СђРSC- РIР»Р°СђС,РёРiРsСђС,С-В»).В РiРё Р·Р°СђС,РµСђРµР¶РµР¶РSPёРNё Р·Р°С...С-Рr СђР»С-Рr СrРSPёРёР°С,Рё РiСђРёРNёРsРjСr СђСrРiР°С,Р°РrРёРSCr РiС-Рr СђР°Сђ РIР°РiС-С,РSPsСђС,С-.

P"PsPrCžPIP°PSPSCІІ PiCḡCžPrPrCḡ

P CrPİP°C,P°PrPëPS PIPëPrC-P»CІC"°C,CHCÍCІCІ PI PjPsP»PsPePs C,PIP°CḡPëPS.
PќPµPIC-PrPsPjPs, C±Pë PiCḡPsPSPëPeP°C" CḡCrPİP°C,P°PrPëPS P· PsCḡPiP°PSC-P·PjCr
PjP°C,PµCḡC-, CІPeP° PiPsPrCÍC" PiCḡCrPrPrCḡ, Cr PjPsP»PsPePs.B PµPsC,CḡC-P±PSPs
PiCḡPëPNëPSCІCІC,Pë CḡC-CëPµPSPSCІC C°°PsPrPs PiCḡPëPiPëPSPµPSPSCІC
PiPsPrCÍPIP°PSPSCІC PiCḡCrPrPrCḡ P°P±Ps PiCḡPëPiPëPSPµPSPSCІC/PIC-PrPjPsPIPë PIC-Pr
P·P°CÍC,PsCÍCrPIP°PSPSCІC CḡCrPİP°C,P°PrPëPSCÍ C-P· CrCḡP°C...CrPIP°PSPSCІC
PePsCḡPëCÍC,C- PIC-Pr PiCḡCrPrPSPsPiPs PIPëPiPsPrPsPICÍPIP°PSPSCІC PrP»CІC PrPëC,PëPSPë
C,P° PePsCḡPëCÍC,C- PIC-Pr C,PµCḡP°PiC-C— PrP»CІC P¶C-PSPePë.

PαPµCḡC,PëP»CHPSC-CÍC,CH

PḡP»C-PSC-C±PSC- PrP°PSC- PiCḡPs PIPİP»PëPI PSP° C„PµCḡC,PëP»CHPSC-CÍC,CH
PIC-PrCÍCrC,PSC-. P"PsCÍP»C-PrP¶PµPSPSCІC PSP° C,PIP°CḡPëPSP°C... CÍPIC-PrC±P°C,CH
PiCḡPs P·PSP°C±PSPµ P·PSPëP¶PµPSPSCІC C„PµCḡC,PëP»CHPSPsCÍC,C- PiCḡPë
PePsPSC†PµPSC,CḡP°C†C-CІC..., PIPëC°°PëC... P·P° PjP°PeCÍPëPjP°P»CHPSC-
C,PµCḡP°PiPµPIC,PëC±PSC- PePsPSC†PµPSC,CḡP°C†C-C— Cr P»CḡPrPëPSPë (PrPëPI.
CḡPsP·PrC-P» B«PαP°CḡPjP°PePsP»PsPiC-C±PSC- PIP»P°CÍC,PëPIPsCÍC,C-B»).B

P—PrP°C,PSC-CÍC,CH PIPİP»PëPIP°C,Pë PSP° CëPIPëPrPeC-CÍC,CH CḡPµP°PeC†C-C— PiCḡPë
PePµCḡCžPIP°PSPSC- P°PIC,PsC,CḡP°PSCÍPiPsCḡC,PsPj P°P±Ps C-PSCëPëPjPë
PjPµC...P°PSC-P·PjP°PjPë.

P'PiP»PëPI CḡCrPİP°C,P°PrPëPSCÍ 10 PjPi PSP° P·PrP°C,PSC-CÍC,CH PePµCḡCrPIP°C,Pë
C,CḡP°PSCÍPiPsCḡC,PSPëPjPë P·P°CÍPsP±P°PjPë C,P° PiCḡP°C†CḡPIP°C,Pë P· C-PSCëPëPjPë
PjPµC...P°PSC-P·PjP°PjPë PSPµP·PSP°C±PSPëPNë. PµCḡPsC,Pµ CÍP»C-Pr P±CÍC,Pë
PsP±PµCḡPµP¶PSPëPj PiC-Pr C±P°CÍ PePµCḡCrPIP°PSPSCІC C,CḡP°PSCÍPiPsCḡC,PSPëPjPë
P·P°CÍPsP±P°PjPë C,P° CḡPsP±PsC,Pë P· PjPµC...P°PSC-P·PjP°PjPë, PrPsPiPsPePë
CḡPµP°PeC†C-CІC PsCḡPiP°PSC-P·PjCr PSP° CḡCrPİP°C,P°PrPëPS PSPµ PIPëP·PSP°C±PµPSP°.

PŸPiPsCÍC-P± P·P°CÍC,PsCÍCžPIP°PSPSCІC C,P° PrPsP·Pë.

P"PsCḡPsCÍP»C- C- PrC-C,Pë PIC-PePsPj PIC-Pr 12 CḡPsPeC-PI

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° бḡ" 10 PjPi (PsPrPSP° C,P°P±P»PµC,PeP°) PsPrPëPS
CḡP°P· PSP° PrPsP±CÍ PSPµP·P°P»PµP¶PSPs PIC-Pr PiCḡPëPNëPsPjCr C—P¶C-.

PµP°C†C-C"PSC,Pë P»C-C,PSCHbPsPiPs PIC-PeCÍ

PµP°C†C-C"PSC,P°Pj P»C-C,PSCHbPsPiPs PIC-PeCÍ CḡCrPİP°C,P°PrPëPS CÍP»C-Pr
P·P°CÍC,PsCÍPsPICÍPIP°C,Pë P· PsP±PµCḡPµP¶PSC-CÍC,Cḡ (PrPëPI. CḡPsP·PrC-P»
B«PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCrPIP°PSPSCІC»).

PµP°C†C-C"PSC,Pë P· PSPëCḡPePsPIPsCḡ P°P±Ps PiPµC±C-PSPePsPIPsCḡ
PSPµPrPsCÍC,P°C,PSC-CÍC,Cḡ

PŞPµCḡPµP· PIC-PrCÍCrC,PSC-CÍC,CH PeP»C-PSC-C±PSPsPiPs PrPsCÍPIC-PrCr
P·P°CÍC,PsCÍCrPIP°PSPSCІC PiCḡPµPiP°CḡP°C,CÍ PiP°C†C-C"PSC,P°Pj P·

РiРsСҫСrС€РµPSPSCПjРё С,,СrPSPeC†C-C— PSPёСҫPsPe P°P±Ps РiРµC‡C-PSPeРё РrP»CП
P»C-PeC†PIP°PSPSCП C,P°PeРёC... РiP°C†C-C”PSC,C-PI РiСҫРµРiР°СҫP°C, PSPµ
СҫРµPePsPjРµPSPrPsPIP°PSPёPNё.

РҫСҫРёPIP°P»C-СГC,СҪ P»C-PeC†PIP°PSPSCП PIPёP·PSP°C‡P°C” P»C-PeP°Сҫ P·P°P»РµP¶PSPs
PIC-Pr C,СП¶P¶PePsСГC,C- C,P° РiРµСҫРµP±C-PiC† P·P°C...PIPсСҫСҫPIP°PSPSCП.
P×C-PeC†PIP°PSPSCП СГP»C-Pr РiСҫРёРiРёPSPёC,Рё РiC-СГP»CП P·PSPёPePSPµPSPSCП
СГРёРjРiC,PsPjC-PI C,P° PIC-PrPSPsPIPёC,Рё РiC-СГP»CП РiPsPIC,PsСҫPSPsPiPs C—C...
PIPёPSPёPePSPµPSPSCП.

P”C-C,Рё.

P”P°PSPёPNё P»C-PeP°СҫСГСҪPeРёPNё P·P°СГC-P± PSPµ СҫРµPePsPjРµPSPrC†C”C,СҪСГCП
РiСҫРёP·PSP°C‡P°C,Рё РrC-C,СПj PIC-PePsPj РrPs 12 СҫPsPeC-PI C‡РµСҫРµP·
PSPµPrPsСГC,P°C,PSC-СГC,СҪ РrP°PSPёC... РiСҫPs P±РµP·РiРµPeC† C,P°
РµC,,РµPeC,РёPIPSC-СГC,СҪ.

РµРµСҫРµPrPsP·CзPIP°PSPSCП.

РќРµ РiPsPIC-PrPsPjP»CПP»PsСГCП РiСҫPs PIPёРiР°PrPeРё РiРµСҫРµPrPsP·C†PIP°PSPSCП
РiСҫРµРiР°СҫP°C,PsPj. PJ C...PsPrC- РrPsСГP»C-PrP¶РµPSPSCП PeP»C-PSC-C‡PSPsC—
P±РµP·РiРµPeРё СҫСrРiР°C,P°PrРёPS РrPsP±СҫРµ РiРµСҫРµPSPsСГРёPIC†CП PI
РrPsP±PsPIC-PNё РrPsP·C- 100 PjPi РiСҫPsC,СПPiPsPj 6 РrPSC-PI.
РќP°PNёРiPsC€РёСҫРµPSC-C€PsCҫ РiPsP±C-C‡PSPсCҫ СҫРµP°PeC†C-C”Cҫ C”
СГPsPSP»РёPIC-СГC,СҪ. РµСҫРё PIPёРiР°PrPePsPIPsPjC† РiСҫРёPNёPsPjC-
PIC†РµСҫРµPrРёPSC† РrC†P¶Рµ PIPёСГPsPeРёC... РrPsP· СҫРµPePsPjРµPSPrPsPIP°PSP°
СГРёРjРiC,PsPjP°C,РёC‡PSP° C,P° РiC-PrC,СҫРёРjC†CҫP° C,РµСҫP°РiC-СП.

РµPsP±C-C‡PSC- СҫРµP°PeC†C-C—.

РµC-Pr C‡P°СГ PeP»C-PSC-C‡PSPёC... РrPsСГP»C-PrP¶РµPSCҫ СҫСrРiР°C,P°PrРёPS,
C,P°P±P»РµC,PeРё РiPs 10 PjPi, P·P°СГC,PsСГPsPIC†PIP°PIC†CП PI P»C-PeC†PIP°PSPSC- 2043
РrPsСҫPsСГP»РёC... C,P° РiC-PrP»C-C,PeC-PI, 120 C-P· СПPeРёC... РiСҫРёPNёPjP°P»Рё
РiСҫРµРiР°СҫP°C, PjC-PSC-PjC†Pj РiСҫPsC,СПPiPsPj СҫPsPeC†.

РќP°PNёРiPsC€РёСҫРµPSC-C€РёPjРё РiPsP±C-C‡PSPёPjРё СҫРµP°PeC†C-СПPjРё РiC-Pr C‡P°СГ
PePsPSC,СҫPsP»CҪPsPIP°PSPёC... PeP»C-PSC-C‡PSPёC... РrPsСГP»C-PrP¶РµPSCҫ P±C†P»Рё
СГPsPSP»РёPIC-СГC,СҪ (9,4 %), РiPsP»PsPIPSPёPNё P±C-P»CҪ (6,9 %) C- PIC,PsPjP° (3,1 %),
P°СГC,РµPSC-СП (1,5 %), СГC†C...C-СГC,СҪ C† СҫPsC,C- (1,2 %),
P·P°РiР°PjPsСҫPsC‡РµPSPSCП (1,03 %).

P’C-P»CҪC€C-СГC,СҪ РiPsP±C-C‡PSPёC... СПPIPёC%, C%Ps
СГРiPsСГC,РµСҫC-PiP°P»РёСГCП РiC-Pr C‡P°СГ PePsPSC,СҫPsP»CҪPsPIP°PSPёC...
PeP»C-PSC-C‡PSPёC... РrPsСГP»C-PrP¶РµPSCҫ, P±C†P»Рё PIC-Pr СГP»P°P±PePsPiPs РrPs
РiPsPjC-СҫPSPsPiPs СГC,СrРiРµPSCП C- P·P°P·PIPёC‡P°PNё PSPµ PIPёPjP°РiP°P»Рё
РiСҫРёРiРёPSPµPSPSCП P»C-PeC†PIP°PSPSCП.

$$P - P_{\pm} P_s P_e C \acute{z} C \acute{e} P_e C - C \acute{t} P \ddot{e} C - P \ddot{e} C - P r C \acute{e} P_e C - C \acute{t} P S P_s C - C, P_e P^{\circ} P S P \ddot{e} P S P \ddot{e}$$

PŷPμCḦPjC-PS PīCḦPēPṽP°C,PSPsCḦC,C-. 3 CḦPSPePē.

PJPjPsPIPë P·P±PμCḡC-PiP°PSPSCI.

P—P±PμCḡC-PiP°C,Pë PI PeP°CḡC,PsPSPSC-PNë PePsCḡPsP±C†C-B PrP»Cḡ P·P°C...PëCḡC,Cr
PIC-Pr CḡPIC-C,P»P°.

P—P±PμCḡC-PiP°C,Pë Cr PSPμPrPsCḡC,CrPiPSPsPjCr PrP»Cḡ PrC-C,PμPNë PjC-CḡC†C-.

PJPiP°PePsPIPeP°.

PμPs 10 C,P°P±P»PμC,PsPe Cr P±P»C-CḡC,PμCḡC-, PiPs 1, 3 P°P±Ps 5 P±P»C-CḡC,PμCḡC-PI Cr
PeP°CḡC,PsPSPSC-PNë PePsCḡPsP±C†C-.

PμPs 15 C,P°P±P»PμC,PsPe Cr P±P»C-CḡC,PμCḡC-, PiPs 2 P±P»C-CḡC,PμCḡP° Cr
PeP°CḡC,PsPSPSC-PNë PePsCḡPsP±C†C-.

PḡP°C,PμPiPsCḡC-Cḡ PIC-PrPiCrCḡPeCr. P—P° CḡPμC†PμPiC,PsPj.

P'PëCḡPsP±PSPëPe.

PkPsCrPePsCḡ PḡPμP»Cḡ, PŸ.Pḡ.

**PḡC-CḡC†PμP·PSP°C...PsPrPḡPμPSPSCI PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPμCḡP°
PjC-CḡC†Cḡ PiCḡPsPIP°PrPḡPμPSPSCI PNëPsPiPs PrC-CḡP»CḡPSPsCḡC,C-.**

PμCḡPsCḡPiPμPeC, P''PμP» PḡP°PjC- P PμPNëP°P», 51-57, PμP°P»P°Cr-PŸPsP»C-C,P° C-
PμP»PμPiP°PjP°PSCḡ, 08184, P†CḡPiP°PSC-Cḡ.